

## Marquette Intellectual Property Law Review

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Volume 15 | Issue 1

Article 1

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# I'm Still Your Baby: Canada's Continuing Support of U.S. Linkage Regulations for Pharmaceuticals

Ron A. Bouchard

*University of Manitoba, Canada*

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# I'M STILL YOUR BABY: CANADA'S CONTINUING SUPPORT OF U.S. LINKAGE REGULATIONS FOR PHARMACEUTICALS

RON A. BOUCHARD\*

ABSTRACT .....	72
INTRODUCTION .....	73
I. REVIEW OF EMPIRICAL STUDIES.....	77
A. <i>Study 1</i> .....	77
B. <i>Study 2</i> .....	83
C. <i>Study 3</i> .....	88
D. <i>Interpretation</i> .....	94
II. ARE THE REGULATIONS A SUCCESS? .....	97
A. <i>Debate Preceding Bill C-91</i> .....	99
B. <i>"Original Policy Intent"</i> .....	107
C. <i>"Patent-Specific" Analysis</i> .....	115
D. <i>Statutory Interpretation</i> .....	121
E. <i>Revisiting the Empirical Data</i> .....	126
III. IMPLICATIONS FOR PHARMACEUTICAL LAW AND POLICY .....	130
A. <i>Theory of Linkage-Based Drug Development</i> .....	130
B. <i>Globalization of Pharmaceutical Linkage</i> .....	133
SUMMARY & CONCLUSIONS .....	143

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\*Dr. Ron A. Bouchard is Visiting Professor in the Faculties of Law and Medicine at the University of Manitoba, Canada. The author is grateful to Richard Hawkins, Joel Lexchin, Alex Stack, and David Vaver for comments on earlier drafts, and to Monika Sawicka, Jamil Sawani, Chris McLelland, Kirsten Burrows, and Cam Sklar for excellent research assistance at varying stages of the work. The study was funded by a career establishment award from the Alberta Heritage Foundation for Medical Research (AHFMR) and a New Investigator Award from the Canadian Institutes for Health Research (CIHR). Correspondence to: ron.a.bouchard@gmail.com.

## ABSTRACT

Canada's linkage regime for pharmaceuticals, modeled after the originating U.S. Hatch-Waxman regime, was brought in under intense political pressure to balance effective patent enforcement over new and innovative drugs with the timely market entry of lower-priced generic competitors. It has been almost two decades since the regulations were enacted, and to date, there has been little objective assessment as to whether the regulations have, in fact, stimulated innovation and timely generic entry. We recently completed three empirical studies on the linkage between drug approval and drug patenting under the Patented Medicines (Notice of Compliance) Regulations (NOC Regulations). Of particular interest was the nexus between the innovative character of new and follow-on drugs approved by Canadian regulators and the scope of intellectual property protection afforded to these drugs via operation of linkage regulations. The first study focused on the type of brand-name and generic drug approvals over an eight-year term following the coming into force of the linkage regime and leading up to the debate on progressive licensing of drug products. The second was an analysis of patenting characteristics for therapeutic products before and after the coming into force of the NOC Regulations. That study also involved a detailed analysis of patent and therapeutic classes in which multinational drug companies are focusing their attention and how these can be used to support various types of new and follow-on drug development. The third was a more nuanced analysis of the innovative nature of new and follow-on drugs approved by regulators over this time frame coupled with an investigation into how patent monopoly periods for pharmaceuticals were extended via the linkage regulations. The implications of the data for the *vires* of pharmaceutical linkage are discussed in light of the stated goals of government to stimulate new and innovative drug development and facilitate timely entry of generic products and, thus, to balance the goals and objectives of food and drug law with those of enabling patent legislation. The Article finishes with a brief description of the global evolution of pharmaceutical linkage and raises issues for further research into local and global systems of pharmaceutical law and policy.

## INTRODUCTION

The Patented Medicines (Notice of Compliance) Regulations (NOC Regulations)<sup>1</sup> came into force in 1993 as part of Canada's perceived obligations under TRIPS and NAFTA to support the domestic pharmaceutical industry.<sup>2</sup> The original policy intent of the regulations, as outlined in successive government Regulatory Impact Analysis Statements (RIAS), was to encourage the development of new and innovative drugs and facilitate the timely market entry of generic drugs, and thus, to balance the goals and objectives of food and drug law with those of patent law. Prior to the linkage regime coming into force, drug regulation and drug patenting represented distinct goals and policy objectives.<sup>3</sup> This balancing exercise is a familiar one to the intellectual property bar owing to the quid pro quo of the traditional patent bargain. Thus, under the terms of the linkage regime, there must be a specific functional legal nexus between approved drugs and patent protection for those drugs pursuant to the NOC Regulations.

As appreciated in the early literature on topic,<sup>4</sup> it was not output metrics but a combination of lobbying by the U.S. pharmaceutical industry, its hopeful domestic university funding partners, and a federal government bent on harmonizing the Canadian system of intellectual

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1. Patented Medicines (Notice of Compliance) Regulations, SOR/1993-133. (Can). [hereinafter Patented Medicines Regulations].

2. North American Free Trade Agreement, U.S.-Can.-Mex., Dec. 17, 1992, T.S. No. 2 (1994), 32 I.L.M. 289 (between the Governments of Canada, Mexico, and the United States; entered into force Jan. 1, 1994) [hereinafter NAFTA]; Trade Related Aspects of Intellectual Property (TRIPS) 1994, Oct. 30, 1947, T.S. No. 27 (1947), 58 U.N.T.S. 187 (negotiated as part of the Uruguay Round (1986-1994) of the World Trade Organization's General Agreement on Tariffs and Trade (GATT) [hereinafter TRIPS]).

3. AstraZeneca Canada Inc. v. Canada (Minister of Health), [2006] 2 S.C.R. 560 (Can.). The Supreme Court of Canada acknowledged that until 1993, the two regulatory systems for drug approval and drug patenting were largely "kept distinct and separate." *Id.* at ¶ 12. Indeed, as late as 2003, Robert Peterson, Director General of the Therapeutics Product Directorate of Health Canada, stated before the Standing Committee on Industry, Science and Technology that the purpose of the drug submission structure was "to support drug review. It was not designed with the aim of safeguarding intellectual property rights." Michael C. Jordan, *The Politics of Drug Patenting in Canada* 102 (Aug. 2005) (unpublished M.A. Thesis, University of Saskatchewan) (on file with the University of Saskatchewan, Electronic Thesis 7 Dissertation Project). Regarding confusion over the precise nature of the approval-patenting nexus, Dr. Peterson stipulated "this in our view is one reason why the linkage aspects of the patented medicines NOC regulations are so hard to grapple with . . . ." *Id.* For a detailed discussion of the political climate leading up the NOC Regulations, see *id.*

4. See generally Robert Tancer, *Foreign Investment in North America and the Pharmaceutical Industry in Canada*, THE INT'L EXEC., Mar./Apr. 1997, at 283; Christopher Scott Harrison, *Protection of Pharmaceuticals as Foreign Policy: The Canada-U.S. Trade Agreement and Bill C-22 Versus the North American Free Trade Agreement and Bill C-91*, 26 N.C. J. INT'L L. & COM. REG. 457, 460 (2000-2001) [hereinafter Harrison].

property with that of the United States that led to enactment of the NOC Regulations. Once the domestic U.S. policy environment was recalibrated away from nascent support for a Canadian-based system of price controls and towards preventing nations such as Canada from having systems of intellectual property law that were perceived to be based on “rights piracy,”<sup>5</sup> stronger patent protection in Canada was inevitable. However, with one notable exception,<sup>6</sup> few independent observers would have guessed during the debate on patent reform that the linkage regime would potentially tip so far to the rights-protection end of the spectrum. It has now been almost two decades since the regulations were enacted subsequent to Canada’s perceived obligations under NAFTA and TRIPS. Given the continuing public debate over high drug prices,<sup>7</sup> the large fraction of research and development carried out by publicly-funded institutions that is ultimately enveloped within commercialized products,<sup>8</sup> and wide criticism of the failings of the patent

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5. This position was strongly advocated by numerous Canadian politicians, particularly those in the governing Conservative Party. *See generally* Harrison, *supra* note 4, at 462–64; JORDAN, *supra* note 3; *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada 7:65–96 (Dec. 1, 1992). For example, Harvie Andre, Minister for Consumer and Corporate Affairs under Prime Minister Brian Mulroney referred to the 1969 bill authorizing compulsory licensing as “legalized theft” and that repeal of the same will indicate that Canada would not be “taking a free ride at the expense of the rest of the world.” Prime Minister Brian Mulroney, apparently bowing to pressure from President Reagan at the time NAFTA was being negotiated, stated that the nation had acted “as a scavenger in the area of intellectual property.” *See e.g.*, Harrison, *supra* note 4, at 513; Alan Story, *Drug Wars: Does Anyone Really Know the Price Tag?*, TORONTO STAR, Dec. 20, 1986, B1; MARCI McDONALD, YANKEE DOODLE DANDY: BRIAN MULRONEY AND THE AMERICAN AGENDA 211 (1995).

6. Dr. Stephen Schondelmeyer, a pharmacologist and health economist, gave evidence before the House of Commons to the effect that it is not the term of single patents that mattered most, but rather how patents add cumulatively to extend market exclusivity, a claim the government at the time vigorously denied. *See infra* Section IV.B. *Compare Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:65–96 (Dec. 1, 1992) and *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:37–40 (Dec. 1, 1992) (testimony of Dr. Stephen Schondelmeyer (Professor, University of Minnesota) and Dr. Elizabeth Dickson (Director General, Department of Industry, Science and Technology)).

7. *See generally* PHILIP J. HILTS, PROTECTING AMERICA’S HEALTH: THE FDA, BUSINESS, AND ONE HUNDRED YEARS OF REGULATION (2003); JERRY AVORN, POWERFUL MEDICINES: THE BENEFITS, RISKS, AND COSTS OF PRESCRIPTION DRUGS (2004); MARCIA ANGELL, THE TRUTH ABOUT THE DRUG COMPANIES: HOW THEY DECEIVE US AND WHAT TO DO ABOUT IT (2004); JAY S. COHEN, OVERDOSE: THE CASE AGAINST THE DRUG COMPANIES (2001).

8. *See generally* SHELDON KRIMSKY, SCIENCE IN THE PRIVATE INTEREST: HAS THE LURE OF PROFITS CORRUPTED BIOMEDICAL RESEARCH? (2003); Ron A. Bouchard, *Balancing Public and Private Interests in the Commercialization of Publicly Funded Medical Research: Is There a Role for Compulsory Government Royalty Fees?*, 13 B.U. J. SCI. & TECH. L. 120, 158–64 (2007); Ron A. Bouchard & Trudo Lemmens, *Commentary, Privatizing*

system to promote innovation,<sup>9</sup> it is an excellent time to assess whether the NOC Regulations have satisfied the twin policy goals of encouraging new and innovative drug development and the timely market entry of generic drugs. We have chosen as the vehicle of our investigation, the growing field of empirical legal research.

The empirical work reviewed and discussed here was designed to investigate whether and how the NOC Regulations have encouraged the development of new and innovative drugs since being enacted. The importance of empirical studies to assessing the efficiency and effectiveness of policy levers such as intellectual property law and regulations cannot be overstated. As noted by some of the most prominent economists, innovation scholars, and patent scholars over the last decades,<sup>10</sup> robust conclusions regarding the consequences for

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*Biomedical Research—a 'Third Way'*, 26 NATURE BIOTECHNOLOGY 31 (2008).

9. MICHELE BOLDRIN & DAVID K. LEVINE, *AGAINST INTELLECTUAL MONOPOLY* 192–96 (2008) (finding only “weak or no evidence” that IP protection increases innovation); KRIMSKY, *supra* note 8.

10. Adam B. Jaffe, *The U.S. Patent System in Transition: Policy Innovation and the Innovation Process*, 29 RES. POL'Y 531 (2000). Jaffe notes that it is possible that the R&D boom in the late 1970s and early 1980s would not have been so large or lasted so long without enhanced IP rights, and that “[i]t is disquieting, however, that there is so little empirical evidence that what is widely perceived to be a significant strengthening of intellectual property protection had significant impact on the innovation process.” *Id.* at 540. Jaffe further observes that “[o]verall, there is a noticeable gap between the highly developed theoretical literature on patent scope and the limited empirical literature.” *Id.* at 548. This is due partially to the infrequency of changes in patent regimes like the one examined by Sakakibara and Branstetter. *Id.* at 546. “Part of the difficulty also lies in the weakness of the connection between the model constructs and quantifiable aspects of a patent regime.” *Id.* at 548. Finally, Jaffe comments, “[t]his limited success is due partially to the difficulty of measuring the parameters of patent policy, and partly due to the difficulty of discerning statistically significant effects when many things have been changing at the same time. But it should surely be viewed as a challenge to researchers to try to do more.” *Id.* at 554. *See also* Roberto Mazzoleni & Richard R. Nelson, *The Benefits and Costs of Strong Patent Protection: A Contribution to the Current Debate*, 27 RES. POL'Y 273, 280 (1998):

The range of arguments about the positive social value of patents is obviously much wider than the area that strong empirical studies explored to date. An analyst, citing the earlier empirical studies that appear to have shown only limited social value, obviously is vulnerable to the argument that those studies do not provide evidence on some of the possibly most important functions patents serve. . . . We cannot present here an empirically supported and intellectually persuasive argument on this broad question. The important empirical research that needs to be done in order to map out the basic facts simply has not been done yet . . . .

*Id.* at 280. BOLDRIN & LEVINE, *supra* note 9, at 192. In a meta-analysis of empirical studies of whether introducing or strengthening patent protection leads to greater innovation, Boldrin and Levine note, “[w]e have identified twenty-three economic studies that have examined this issue empirically. . . . The executive summary: these studies find weak or no evidence that strengthening patent regimes increases innovation; they find evidence that strengthening the patent regime increases . . . patenting!” *Id.*

technological innovation of changes in patent law and policy are few and far between. This is due primarily to a fundamental lack of relevant empirical data. The same applies in the reverse, as governments have specific legal and policy goals in mind when drafting law and regulations, which are then reviewable by the courts in judicial review proceedings.

We have recently published three studies that provide empirical data for analysis of whether pharmaceutical linkage regulations, *in operation*, are consistent with the intent of balancing the goals of patent law with those of food and drug law, while stimulating new and innovative drug development. The data are relevant to all jurisdictions that have, or are currently contemplating bringing in, some form of linkage. The first study focused on the types of new and follow-on drugs approved by Canadian regulators between 2001 and 2008.<sup>11</sup> The year 2001 was chosen as our starting point, as this was the date when substantial amendments to Canadian drug regulation were made that affected both the mechanisms and speed of approval.<sup>12</sup> The second study focused on patenting patterns associated with drugs identified in the first study.<sup>13</sup> We analyzed the number of patents per drug, the number of patents listed on the patent register, and the timing of these metrics to one another and the date of drug approval. We conducted tests on the statistical nature of the trends in patenting before and after the NOC Regulations came into force. In addition, we analyzed patents and approved drugs in terms of the World Health Organization (WHO) Anatomic Therapeutic Class in order to identify therapeutic areas (cardiovascular, cancer, etc.) in which firms are focusing their drug development activities. Finally, we developed an independent patent classification scheme to analyze the type (chemical, use, combination, etc.) of patents associated with approved drugs. The third study focused on the legal nexus between drug approval and drug patenting in a subgroup of the most profitable drugs sold in Canada.<sup>14</sup> Our aim was to quantify patenting, patent listing, and patent litigation patterns associated with these drugs under the NOC Regulations and to investigate the manner in which patent terms on already approved

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11. Monika Sawicka & Ron A. Bouchard, *Empirical Analysis of Canadian Drug Approval Data 2001–2008: Are Pharmaceutical Players “Doing More With Less”?*, 3 MCGILL J.L. & HEALTH 85 (2009).

12. *Id.* at 107.

13. Ron A. Bouchard, Richard W. Hawkins, Robert Clark, Ray Hagtvedt, & Jamil Sawani, *Empirical Analysis of Drug Approval–Drug Patenting Linkage for High Value Pharmaceuticals*, 8 NW. J. TECH. & INT. PROP. 174 (2010) [hereinafter Bouchard 2010].

14. Ron A. Bouchard, Jamil Sawani, Chris McLelland, Monika Sawicka & Richard W. Hawkins, *The Pas de Deux of Pharmaceutical Regulation and Innovation: Who’s Leading Whom?*, 24 BERKELEY TECH. L.J. 1461, 1463 n.2 (2009) [hereinafter Bouchard 2009].

blockbuster drugs were extended via operation of the linkage regime. The purpose of the present Article is to review data from these studies and to analyze them in light of the stated objectives of the NOC Regulations as well as relevant Supreme Court of Canada jurisprudence and principles of statutory interpretation.

## I. REVIEW OF EMPIRICAL STUDIES

### A. Study 1\*

Our first study (“Study 1”)<sup>15</sup> was an analysis of drug approvals, referred to in Canada as Notices of Compliance (NOCs), issued over the period from 2001 to 2008. Our goal was to develop an independent empirical methodology and synthetic model to investigate what types of drug candidates were approved by Canadian regulators over nearly a decade and to investigate which type of drugs might qualify for flexible departure under emerging lifecycle-based drug regulatory models.<sup>16</sup> A related goal was to use this model to identify patterns in the rate (how much) and direction (what kind) of innovative activity by domestic brand name and generic pharmaceutical firms. One methodological tool employed by our group was construction of “patent trees.” Patent trees were used to assess the number, type, and timing of patents granted in relation to a specific drug or a group of related follow-on drugs, and these patent trees could be assessed and visualized. An example of such an analysis is provided in Fig. 1.

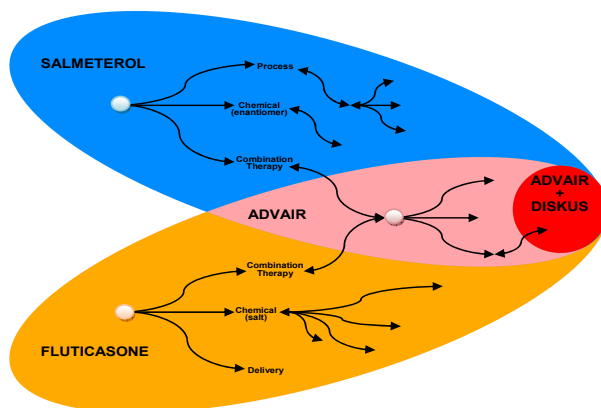
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\* For the full study, please refer to Monika Sawicka & Ron A. Bouchard, *Empirical Analysis of Canadian Drug Approval Data 2001–2008: Are Pharmaceutical Players “Doing More With Less”?*, 3 MCGILL J.L. & HEALTH 85 (2009).

15. See generally Sawicka & Bouchard, *supra* note 11.

16. This is referred to in Canadian pharmaceutical policy as “progressive licensing.” See generally HEALTH PRODUCTS AND FOOD BRANCH, BLUEPRINT FOR RENEWAL: TRANSFORMING CANADA’S APPROACH TO REGULATING HEALTH PRODUCTS AND FOOD, 33 (2006), [http://www.hc-sc.gc.ca/ahc-asc/alt\\_formats/hpfb-dgpsa/pdf/hpfb-dgpsa/blueprint-plan-eng.pdf](http://www.hc-sc.gc.ca/ahc-asc/alt_formats/hpfb-dgpsa/pdf/hpfb-dgpsa/blueprint-plan-eng.pdf) [hereinafter HEALTH CANADA, BLUEPRINT]. See also Progressive Licensing Project, Health Canada, The Progressive Licensing Framework Concept Paper for Discussion (2006), [http://www.hc-sc.gc.ca/dhp-mps/alt\\_formats/hpfb-dgpsa/pdf/prodpharma/proglic\\_homprog\\_concept-eng.pdf](http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/proglic_homprog_concept-eng.pdf) [hereinafter HEALTH CANADA, PLF CONCEPT PAPER]; Neil Yeates et al., *Health Canada’s Progressive Licensing Framework*, 176 CAN. MED. ASS’N J. 1845, 1845 (2007).





**Fig 1. Example of Search String and Patent Tree Analysis for Advair Diskus®.** Patents were identified using the specific and general search strings described in the Methods. In addition to quantifying patents per drug, this method also allows assessment of how specific drugs evolve into related drug forms or (in this case) drug products representing combinations of known drugs. In addition, the patent tree analysis allows for identification of relevant patent types based on the classification nomenclature described in the Methods. Finally, the patent tree analysis provides data relating to drug development, but also on the type of patents selected by pharmaceutical companies for listing on the patent register in order to prevent generics. Reproduced courtesy of the *Northwestern Journal of Technology and Intellectual Property*. ©

We analyzed 3,837 drug approvals over the period from 2001 to 2008, with a particular focus on the types of new and follow-on drugs being approved and the manner in which approvals were consistent with emerging lifecycle models of drug regulation.<sup>17</sup> Of the cohort of 3,837 approvals, 45% were administrative in nature (product manufacturer or name change), leaving 2,122 approvals for detailed analysis. There were two related components of the work that were published in separate articles. The first focused on approval statistics, whereas the second focused on the innovative character of approved drugs.

Data from the first component demonstrated that the percentage of new drugs developed over the test period decreased substantially whereas the number and fraction of follow-on drug increased. All three groups in the “new drug” category investigated experienced a decrease over time. This included new drug submissions (NDSs) generally, and NDS submissions containing a new active substance (NAS) and those directed to First in Class drugs.

By contrast, all four categories of “follow-on” drugs increased over

17. Sawicka & Bouchard, *supra* note 11, at 104. See also Hans-Georg Eichler et al., Opinion, *Balancing Early Market Access to New Drugs with the Need for Benefit/Risk Data: A Mounting Dilemma*, 7 NATURE REVIEWS: DRUG DISCOVERY 818, 823–24 (2008).

the same time frame, sometimes dramatically. Of the four groups followed, two represented brand-name submission classes (standard supplementary new drug submissions (SNDS) and First in Class SNDSs), and two represented generic submissions (standard abbreviated new drug submissions (ANDS) and supplemental ANDS, or SANDS). SNDSs, also known as “line extensions” of previously existing products, usually involve changes to a pre-existing drug such as a change in the route of administration (e.g., oral to intravenous), dosage form (e.g., tablet to capsule), salt form (e.g., besylate to mesylate), or indication (e.g., antidepressant to anxiolytic). For the most part, getting a line extension or SNDS onto the market is a faster process compared with drugs approved via the new drug submission stream. This is true even where approval times for SNDS and NDS are roughly equal, as production and marketing of line extension products takes less time than producing and marketing truly new drugs, owing to manufacturing experience and related competencies.

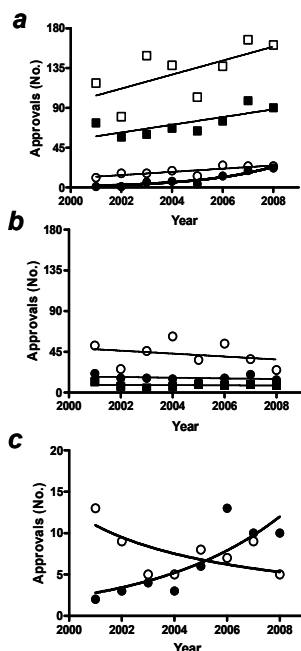
Drugs approved via NDS and SNDS routes can be classified as either First in Class or Me Too. For the NDS route, First in Class drugs are those that contain either a new ingredient or are directed to a new use (or indication), whereas NDS Me Too drugs neither contain a new ingredient nor are directed to a new use, but do have an improved benefit/risk profile. For the SNDS route, relatively small changes to existing chemical structures such as salts or isomers may still yield First in Class or Me Too designations. The difference is that while both SNDS First in Class and Me Too drugs can cover new chemical forms, drugs directed only to a new use may be deemed First in Class SNDSs, while those that do not are deemed Me Too. Because even a follow-on First in Class must be directed to a new use as opposed to just a new chemical form with altered benefit/risk, a higher level of innovation is typically ascribed to follow-on First in Class as opposed to Me Too drugs.<sup>18</sup>

One of the most intriguing findings of Study 1 is that the number of new Me Too and First in Class NDS NOCs decreased slightly over the test period. By contrast, the number of follow-on Me Too SNDS and First in Class SNDS NOCs increased significantly. Me Too SNDS NOCs in particular doubled over the test period. Moreover, First in Class SNDS NOCs increased in a strongly time-dependent manner,

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18. For a comparison of Canadian and WHO First in Class and Me Too classifications schemes, see Sawicka and Bouchard, *supra* note 11, at 108. “[U]nder the WHO methodology, compounds that are in the same chemical family as the original First in Class drug are all deemed to be Me Too drugs irrespective of whether they are directed to the new indications.” *Id.*

from a single drug in 2001 to twenty-two drugs in 2008. The slope of this increase over time well exceeds even that for generic supplemental submissions.



**Fig 2. Shifting Patterns of Drug Approval and Drug Regulation During the Period 2001–2008.** a. Market authorizations for several types of follow-on drugs increased over the 2001–2008 test period. This includes, brand-name Supplemental New Drug Submission (SNDS; □) and SNDS First In Class (SNDS FIC; ●) approvals, and generic Abbreviated New Drug Submission (ANDS; ■) and follow-on Abbreviated New Drug Submission (SANDS; ○) approvals. b. In contrast, approvals granted to brand-name firms for “new” drug submissions declined from a smaller baseline over the same period. This included approvals from New Drug Submission (NDS; ○), New Active Substance (NAS; ●) and NDS First In Class (NDS FIC; ■) streams. c. Expedited review pathway for drug approval is shifting towards probationary-type approval consistent with emerging lifecycle models of regulation. Expedited drug approvals with no post-market evidentiary obligations (Priority Review; ■) decreased over the 2001–2008 test period while those with significant post-market obligations conditions (NOC/c; ●) increased steeply over the same time frame. Reproduced courtesy of the *Berkeley Technology Law Journal*. ©

Together with data showing a decline in all types of new or standard submissions by brand-name firms and an increase in other types of supplementary submissions assessed, these results suggest that the Canadian pharmaceutical industry is expending increasingly fewer of its resources on developing novel “first-of-kind” technologies, more on leveraging existing technologies. As such, technology appropriation is

alive and well in Canada.<sup>19</sup>

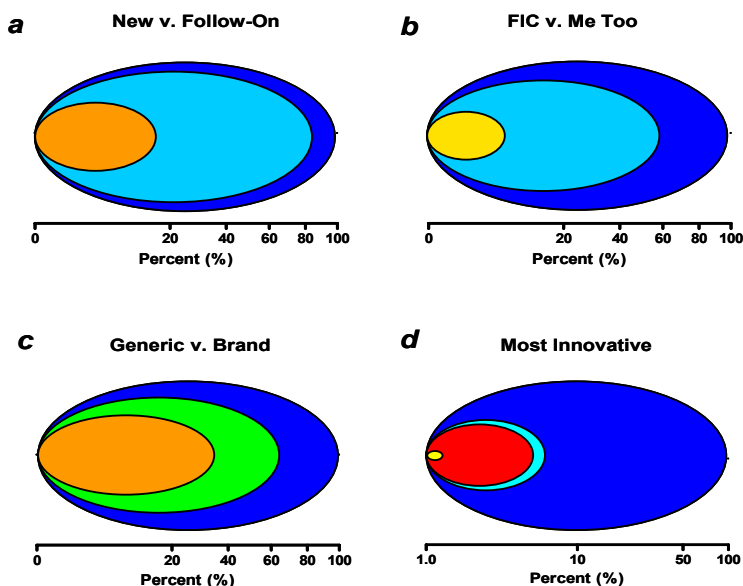
The data from Study 1 suggest that the trend toward the “flexible departure” limb of the emerging lifecycle model of drug regulation is being accompanied by a small but significant trend for sponsors to meet conditions associated with NOC/c approval (Fig. 3). This conclusion is tempered, however, by the large number of outstanding NOC/c approvals where the conditions have not yet been met. A second caveat is the fact that there is not a great deal of data in this regard, given the gap between issuance and conditions met in later years, which does not apply to analysis of approvals per se. The observation that an increasing number of drugs are being made available to the public under the circumstance that they meet certain conditions in order to maintain market authorization demonstrates that Health Canada is already approving drugs with the Progressive Licensing Framework (PLF) in mind. Positively, to date none of these drugs have been recalled for safety reasons.

The second limb of Study 1 focused on the innovative character of approvals granted between 2001 and 2008.<sup>20</sup> As with the initial study, our goal was to develop an independent method to quantify patterns in innovative activity by pharmaceutical firms and to analyze this data in relation to regulatory incentives designed to encourage pharmaceutical innovation via provision of strong patent rights. The work was specifically designed to probe the functional and structural link between drug approval, drug patenting, drug litigation, and innovation.

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19. As used here, the term “appropriation” refers to a party’s ability to capture profits generated from their own inventions or related inventions. *See generally* David J. Teece, *Profiting from Technological Innovation: Implications for Integration, Collaboration, Licensing and Public Policy*, 15 RES. POL’Y 285 (1986).

20. Bouchard 2009, *supra* note 14.



**Fig. 3. Profile of Pharmaceutical Innovation in Canada between 2001–2008.** *a.* New v. follow-on approvals. Of total drugs approved over the test period, 15% constituted New Drug Submissions (NDS: ●) while 84% were for follow-on drugs (SNDS, ANDS and SANDS: ●). *b.* Types of follow-on approvals. Of follow-on approvals, 6.1% were for supplementary “First in Class” (SNDS FIC: ●) drugs while 59% were for Me-Too drugs (●). *c.* Brand name v. Generic approvals. Of all drugs approved during the test period, 65.5% of approvals were granted to brand name drug companies (NDS and SNDS: □) and 34.5% to generic companies (ANDS and SANDS: ●). *d.* Most innovative drugs. While 6.5% of approvals during the test period were directed to New Active Substances (●; NAS) and 5.3% of all NDS and SNDS submissions were approved under an expedited review process (●; Priority Review and NOC/c), only 1.23% of all drugs approved over the period 2001–2008 were also directed to FIC therapies and contained a NAS (●). Areas are approximations of calculated means for the entire test period. Note that area scales are linear for panels *a-c* and log for panel *d*. Reproduced courtesy of the *Berkeley Technology Law Journal*.<sup>6</sup>

The data revealed that the number of truly innovative drug products was very small, amounting to just 1.87% of all approvals granted to brand-name drug companies over the eight-year test period. The largest fraction of drug development was directed to Me Too drugs (59%), while follow-on drugs as a whole represented 85% of all approvals over the test period. By contrast, the percentage of approvals that either contained an NAS that was directed to a First in Class drug, even irrespective of whether First in Class drugs were approved via the new (NDS) or follow-on (SNDS) approval pathways, or that underwent some form of expedited review was only 6.5%, 6.4%, and 5.3% of all approvals granted between 2001 and 2008, respectively. The largest category for new drugs assessed was for NDS approvals, and even then

only 16% of all approvals went through this mechanism; the remaining drugs were approved via SNDS and generic pathways. The data illustrate that drug companies are focusing their efforts primarily on follow-on drug development, and that this effort was rewarded by Canadian regulators with large numbers of approvals directed to these products.

Our qualitative findings on pharmaceutical innovation in Canada parallel those observed in other jurisdictions, including the United States.<sup>21</sup> That is, the multinational pharmaceutical industry appears to be leaning away from breakthrough drug development, towards less innovative products referred to variously as follow-on, incremental, supplemental, line extension, Me Too, and bioequivalent drugs. While our data do not speak directly to claims that diminished innovation is due to the loss of “low hanging fruit”<sup>22</sup> or spiraling costs of drug development,<sup>23</sup> we argue the results provide a third plausible explanation for the diminution of breakthrough product development. That is, innovation policy and drug regulation that are strongly dependent on intellectual property rights can profoundly shape the rate and direction of innovative activity by multinational firms *antecedently*, towards incentives provided for by law and away from truly breakthrough products under conditions where the two do not coincide.

### B. Study 2\*

In our second study (“Study 2”),<sup>24</sup> we set out to empirically analyze

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21. See, e.g., John Abraham & Courtney Davis, *A Comparative Analysis of Drug Safety Withdrawals in the UK and the US (1971–1992): Implications for Current Regulatory Thinking and Policy*, 61 SOC. SCI. & MED. 881 (2005); Editorial, *European and French Pharmaceutical Market Assessed by Prescrire in 2005: Mainly Bogus Innovation*, 30 FARMACIA HOSPITALARIA 68 n.2 (2006) [hereinafter *Bogus Innovation*]; Kenneth I. Kaitin et al., *Therapeutic Ratings and End-of-Phase II Conferences: Initiatives To Accelerate the Availability of Important New Drugs*, 31 J. CLINICAL PHARMACOLOGY 17 (1991); Domenico Motola et al., *An Update on the First Decade of the European Centralized Procedure: How Many Innovative Drugs?*, 62 BRIT. J. OF CLINICAL PHARMACOLOGY 610 n.5 (2006); *Drugs in 2001: A Number of Ruses Unveiled*, 11 PRESCRIRE INT’L 58, 58 (2002) [hereinafter *Drugs in 2001*]; NAT’L INST. FOR HEALTH CARE MGMT., *CHANGING PATTERNS OF PHARMACEUTICAL INNOVATION* 1, 7–14 (2002) [hereinafter *PHARMACEUTICAL INNOVATION*]; *New Medicines in 2007: Regulatory Agencies and Policy Makers Leave Public Health in the Hands of the Pharmaceutical Industry*, 17 PRESCRIRE INT’L 78 n.94 (2008) [hereinafter *New Medicines in 2007*].

22. Fredric J. Cohen, Opinion, *Macro Trends in Pharmaceutical Innovation*, 4 NATURE REV. DRUG DISCOVERY, Jan. 2005, at 78 [hereinafter Cohen 2005].

23. Joseph DiMassi et al., *The Price of Innovation: New Estimates of Drug Development Costs*, 22 J. HEALTH ECON. 151, 152 (2003).

\* For the full study, please refer to Ron A. Bouchard, Richard W. Hawkins, Robert Clark, Ray Hagtvædt, & Jamil Sawani, *Empirical Analysis of Drug Approval–Drug Patenting Linkage for High Value Pharmaceuticals*, 8 NW. J. TECH. & INT. PROP. 174 (2010).

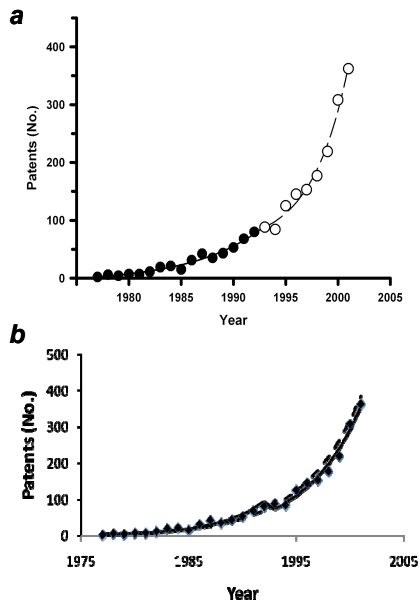
drug patenting patterns for high value drug candidates. We investigated patenting and listing data associated with ninety-five drugs approved between 2001 and 2008. Data were analyzed with regard to five categories: (1) the entire cohort of drugs (Cohort;  $n=95$ ), (2) the most profitable drugs by sales (Most Profitable;  $n=33$ ), (3) the drugs approved via an expedited approval process without significant post-market conditions (Priority Review;  $n=40$ ), (4) the drugs approved via expedited approval with significant post-market conditions (NOC/c;  $n=16$ ), and (5) the drugs approved via the Priority Review stream that were also approved with significant post-market conditions (PR-NOC/c;  $n=6$ ). Drugs were, therefore, split into categories representing drugs already vetted by the market to be blockbuster in nature, and those that were granted expedited review status by regulators in the hopes they would be blockbusters. For the sake of simplicity, only results pertaining to the cohort are presented here.

The cohort was associated with 3,850 patents, resulting in a large average patent per drug ratio of 40:1. In other words, each drug studied was associated with at least 40 patents. Of these, 196 (5%) were listed on the patent register to prevent generic entry under the NOC Regulations. Patenting activity per drug took place over a relatively long period of thirty-five years. The time required for peak patenting per drug progressively declined over the course of 1977 to 2000, from about twenty-five years to eight years. Averaged patenting activity, expressed as year after first instance, exhibited a significant plateau over an eight year period, between eight and sixteen years after the year of first instance. During this time, peak patenting was maintained at an average of about 2.5 patents per drug per year.

Statistical fits to the data suggest there were two components of pharmaceutical patenting in between 1977 and 2001; a slower and smaller amplitude component up to 1993 and a larger and faster component following 1993. As illustrated by the data in Fig. 4, the amount of patenting was approximately 2.5 times greater and 2.0 times faster between 1993 and 2001 than patenting patterns from 1977 to 1993. Given that the break in patenting activity in 1993 coincides with the coming into force of the NOC Regulations, the results strongly suggest that the linkage regime itself has substantially influenced both the degree and rate of patenting activity by brand-name pharmaceutical firms.

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24. See Bouchard 2010, *supra* note 13.



**Fig 4. Fit of Cohort Patenting Data to Exponential Functions.** Data were fit to two single exponential functions using two different procedures. In panel *a*, data were split into two epochs; 1977–1993 (●) and 1993–2001 (○), the point of maximal rate of increase in patenting activity. Data were then fit to a sum of two single exponential 4 parameter functions of the form  $A \cdot \exp(b \cdot (Y - d)) + B$ , where  $A$  is amplitude,  $B$  is the rate constant of the exponential function and  $Y$  is calendar year. Solid and dashed lines are fits to epochs one and two, respectively. Amplitudes and time constants were 12.60 0.1467 and 30.24 and 0.2875 for the first and second epochs respectively. The fits suggest the presence of a small and slower phase of patenting followed by a larger and faster phase. In panel *b*, linear regression analysis was undertaken to probe whether a year-specific change in the patent regime in 1993 resulted in a second exponential function. We assumed a data generating process with the functional form:  $Y = \exp[(0 + 1 I)t + \epsilon]$ , where  $Y$  is total patents,  $\epsilon$  is a noise term with zero mean and constant variance,  $t$  is the year, and  $I$  is an indicator variable taking on the value 1 for year 1993 and later, and zero otherwise. A log transform allowed testing of the null hypothesis ( $1 = 0$ ) using linear regression. The result ( $p = 0.006955$ ) suggests there is a shift in the exponential growth of patenting in 1993. Raw data (◆) are the same as those in *a*. Reproduced courtesy of the *Northwestern Journal of Technology and Intellectual Property*.<sup>o</sup>

We next investigated changes in global patterns of peak patenting per drug for the cohort. We analyzed changes in the average time it took for peak patenting per drug over the course of the period 1977–2000 for the 95 drugs in the cohort. Data are expressed as the time after the year of first issuance of a patent for a given drug. This was done to probe the patenting strategy of pharmaceutical firms over the test period.

During the first four years of the test period (1977–1980) the average year to peak patenting activity was about twenty-five years. For the five years between 1986 and 1991, this value decreased to about fifteen years, and decreased further again to eight years for the five-year period



between 1996 and 2000. Thus, there was a reduction of the time to peak patenting from a maximum of twenty-five years in 1979 to a minimum of 7.5 years in 2000. This equals a 70% increase in the speed of maximal patenting per drug over the course of twenty years. While this conclusion is somewhat tentative given the lower numbers of patents towards the end of the test period, the data suggest that pharmaceutical firms have become significantly more efficient in their patenting efforts over time. This conclusion is supported by the substantial growth in patent listing in the last decade, the convergence of patenting and patent listing data, and the decreasing time lag between drug approval and drug patenting and patent listing.

Data in Study 2 were also analyzed within the context of patent type (chemical, use, etc.) and therapeutic (cardiovascular, antibiotic, etc.) classification schemes, the former of which was developed for this study. Patent classifications were calculated based on whether patent claims were directed to given content. The results demonstrate significant preferences in the various groups towards discrete therapeutic and patent classifications. Indeed, the cohort was associated with a vast array of both patent and WHO therapeutic classifications. There were 5,859 individual patent classifications on the cohort, which amounted to an average of 61 patent classes per marketed drug. These were distributed widely across patent types, with particular concentrations for Combination Therapy, Use and Administration patents, and a second large grouping for Chemical and Process patents. The results on therapeutic classifications indicated a relatively narrow scope of therapeutic targets, with strong overlap between therapeutic classes identified in the study and those with the highest domestic sales in Canada.

Results from the patent classification study are particularly relevant to analysis of the validity of the NOC Regulations. Readers may be reminded that the two main regulatory mechanisms underpinning follow-on innovations are the wide definition of a NAS and the wide scope of uses and chemical derivatives permitted under the SNDS stream. For example, a NAS may include isomers, derivatives, or salts of chemical substances already approved for sale or biological substances previously approved but differing in molecular structure, nature of the source material, or even manufacturing process.<sup>25</sup>

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25. Memorandum from E. Somers on New Active Substances to Health Canada (June 4, 1991), [http://www.hc-sc.gc.ca/dhp-mps/alt\\_formats/hpfb-dgpsa/pdf/prodpharma/nas\\_nsa\\_pol-eng.pdf](http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/nas_nsa_pol-eng.pdf) [hereinafter Health Canada, New Active Substances]; Health Canada, Notice of Compliance (NOC) Database Terminology (Oct. 1 2004), [http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/noc-acc/term\\_noc\\_acc-](http://www.hc-sc.gc.ca/dhp-mps/prodpharma/notices-avis/noc-acc/term_noc_acc-)

Similarly, an SNDS may be filed for changes to a drug that is already marketed by a sponsor: including minor changes to dosage, strength, formulation, manufacture, labeling, route of administration, or use/indication.

Either of these two approval pathways would be consistent with what we have termed a “paradoxical approval-patent linkage,” whereby pharmaceutical firms game the linkage system in order to obtain the largest patent protection under the NOC Regulations for the products with the lowest levels of innovation. The patent classification data observed here show that the patent pool supporting submissions directed to the SNDS approval stream is very large, as is the pool for other approval types with narrow filing requirements (NAS, NOC/c, Priority Review; SNDS First in Class). Similarly, the therapeutic classification data indicate that firms are innovating in relatively low-risk areas with established market presence. In addition to supporting follow-on drug submissions, a wide array of patent classifications, particularly for combination, use and chemical derivative patents, would also provide fodder for listing on the patent register. A broad array of patents can increase the market exclusivity period of blockbuster drugs about to come off patent by either providing for further related follow-on drug submissions, or increasing the pool of “relevant” patents for listing on the patent register.

Combined, the data in Study 2 demonstrate that firms are able to identify attractive drug candidates both after regulatory approval and during the approval process. During the approval stage, firms begin the process of layering patents, listing patents on the patent register, and obtaining further patents with broad classifications to expand the boundary of legal protection afforded by the patent and linkage regulation regimes. Broad patent classification in particular allows firms to fill offers with candidates for later follow-on submissions and patent listing candidates.

A final observation from Study 2 is that the linkage regime, acting in combination with both the traditional patent system and the existing drug approval framework, has proven to be a highly flexible tool in the hands of sophisticated pharmaceutical firms. For example, the combination of the speed of patent listing compared with patenting and the relatively low relevance requirement for listing has enabled pharmaceutical firms to rapidly identify attractive drug targets for legal protection even during the regulatory approval stage, particularly for drugs undergoing some form of expedited approval.

Identification of drugs for “rights layering” early in the approval stage rather than later further serves the significant function of reducing the regulatory lag at the front end of the product lifecycle while at the same time extending market exclusivity at the end of a product lifecycle. Together, the results from Study 2 show strong, increasing, and faster utilization of both patent and linkage regulation regimes for high value pharmaceuticals over time, particularly for drugs undergoing some form of expedited approval.

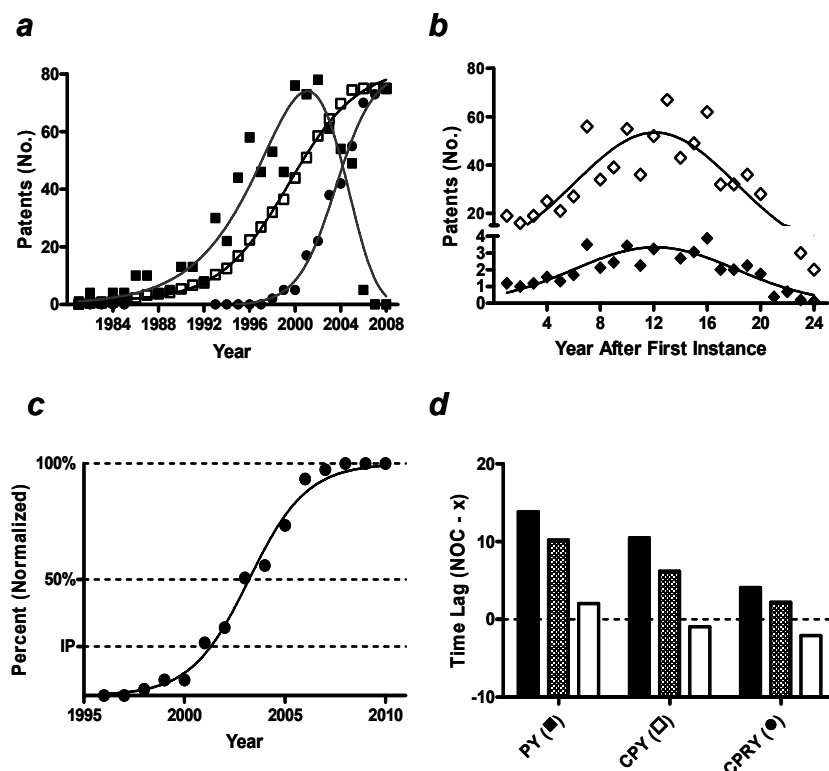
*C. Study 3\**

Our third study (“Study 3”)<sup>26</sup> was focused on the functional linkage between approved drugs and extended patent protection afforded by the NOC Regulations in a subgroup of the most profitable drugs in Canada (n=16). We chose the top sixteen drugs for our initial study because this cohort was likely to display the strongest patenting and patent listing patterns. Pharmaceutical companies have a vested interest to protect the market on their most profitable drugs, and the primary means of doing so is via patenting. Each of the drugs studied under the patent analysis were approved between 2001 and 2008 and were analyzed as part of Study 1.

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\* Ron A. Bouchard, Jamil Sawani, Chris McLelland, Monika Sawicka & Richard W. Hawkins. *The Pas de Deux of Pharmaceutical Regulation and Innovation: Who's Leading Whom?*, 24 *BERKELEY TECH. L.J.* 1461, 1463 n.2 (2009).

26. Bouchard 2009, *supra* note 14.



**Fig 5. Patenting and Patent Listing Patterns Associated with Drug Approval.** a. Total patents issued by year associated with a subset of sixteen top selling drugs (■); cumulative number of patents associated with the subset (□); and cumulative number of patents listed on the patent register under linkage regulations associated with the subset (●). Note the strong convergence of total and listed patents over the course of the test period. b. Total (◇) and average (◆) number of patents on approved drugs within the subset plotted as a function of the time after the priority date on which the first patent on the subset was issued. c. Method used to calculate the temporal gap between the date of mean drug approval on the patent subset (2005) and the inflection point (IP), 50th and 100th percentile of normalized maximum drug patenting and approvals. Data are from the cumulative number of patents (●) above. d. Graph expressing the temporal relationship between drug approval and the IP, 50th and 100th percentile of maximal normalized patents granted per year (PY), cumulative patents per year (CPY), and cumulative patents listed on the patent register per year (CPRY). Time points are calculated as the difference between the date of drug approval (NOC) and the date of the IP, 50th and 100th percentile (NOC-x). The data suggest drug patent listing is a better proxy for drug approval than drug patenting. Reproduced courtesy of the *Berkeley Technology Law Journal*.©

Patents granted on the approval subset had a bell-shaped distribution over time, peaking in 2001. There were a total of 772 patents on the 16 drug products. As illustrated in Fig. 5a, this corresponded to an average patent per product ratio of 48:1. That is, there was an average of 48 patents for each drug in the subset analyzed. The fastest rate of grant occurred between approximately 1993 and 2001. Patenting reached a plateau by 2004. When expressed as year

after first instance (Fig. 5b), patenting grants can be seen to occur over a twenty-five year period on average. Listing data is also provided in Fig. 5a. As expected, it lags behind patenting activity. However, listing activity catches up quickly, as indicated by the convergence of the two curves over time.

Study 3 also investigated the temporal relationship between NOC grants, patent issue, and patent listing in some detail. We found there was a significant lag between the date on which NOCs were granted and the dates on which patents of the same drug product were granted. This pattern was observed independent of whether patents were expressed by year of grant or cumulatively. This is not surprising in light of the regulatory lag between drug patenting and drug approval. However, the data were different for patent listings. As shown in Fig. 5d, the average data for both the inflection point (the point at which the data significantly depart from baseline) and the fiftieth percentile of maximum exceeded the null point by only four and two years, respectively. This lag can be compared with that of ten and eight years for patenting data. Of interest, the calculated values for the fiftieth percentile and peak patent listing were only one to two years on either side of the null point. In other words, there was virtually no significant lag between drug approval and patent listing as the test period progressed from 2001 to 2008.

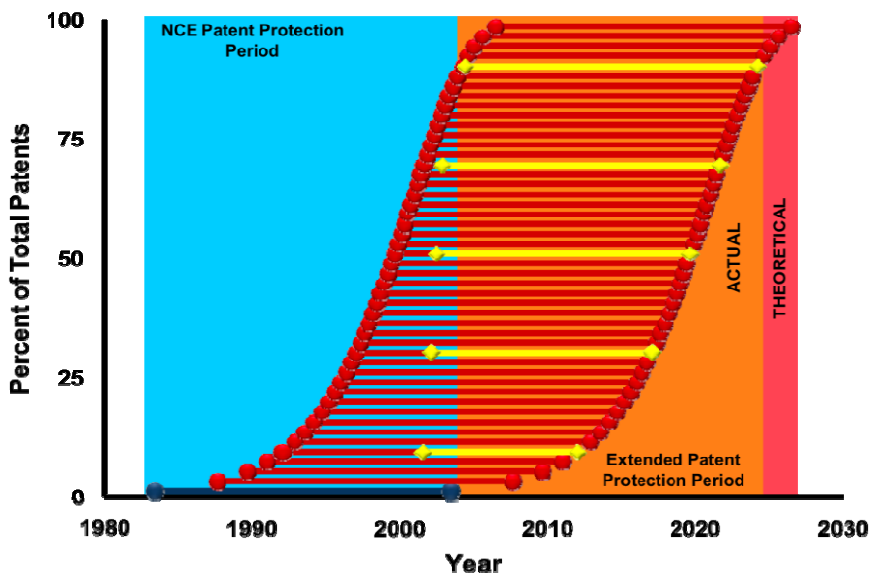
Data from the analysis described above suggest that patent listing under the NOC Regulations appears to have evolved over time to be a better proxy for drug development than drug patenting per se. This result suggests that while patenting data remains an important reflection of innovation incentives for domestic pharmaceutical companies, patent listing may have evolved into a more contextually relevant indicator of drug development in Canada.

While the idea that patent listing may better reflect firm drug development strategy under pharmaceutical linkage, this analysis does not reflect on trends for new and follow-on drugs specifically. We therefore further explored the link between the timing of new and follow-on drug approvals, expedited drug approvals, and associated drug patenting, patent listing and litigation. In this analysis, drug patenting and listing were assumed to represent incentives for innovation whereas expedited drug approval was taken as a measure of lifecycle-based regulatory incentives for innovation. In particular, we compared fitted curves for cumulative patenting and patent listing activity as well as that for expedited approval against concomitant fits to new and follow-on drug approvals. The data indicated that neither the steep time-dependent changes in patent grant, patent listing, nor

NOC/c-type approval (expedited approval with significant post-marketing evidentiary requirements) were correlated with, and thus, may not provide a measurable incentive for, pioneering drug development. Patenting, patent listing, and NOC/c approvals were all strongly non-linear in nature (i.e., occurring very rapidly) compared with the slow linear changes in both new and follow-on drug approvals. The three trends could be observed to occur either before or during those for new and follow-on drug development.

The observations from the analysis above suggest that neither patenting, patent listing, nor emerging lifecycle-based models of drug regulation appear to have provided significant incentives for new drug development in Canada. Results such as these support the conclusion that the NOC Regulations provide a stronger incentive for follow-on rather than pioneering drug development.

One of the most important observations of Study 3 was that the linkage regime can, in the hands of sophisticated firms, essentially double the cumulative term of patent protection on drug products. As demonstrated by the dark blue symbols and line in Fig. 6, the average period of patent protection associated with the “originating patent” was about twenty years, from 1983 to 2003. This represents an average of patent terms before (seventeen years from date of grant) and after (twenty years from filing date) amendments made to patent legislation pursuant to TRIPS. By comparison, the duration of cumulative protection on the subset of most profitable drugs was about two-fold longer, lasting from about 1987 to 2026. This yields a term of extended patent protection, due solely to operation of linkage regulations, of about forty-three years per drug on average. The primary basis for this extension is the cumulative life of patents deemed legally relevant to the original product that were listed on the patent register to prevent generic entry. The averaged results from the sixteen drugs studied are shown in Fig. 6 below.



**Fig. 6. Extension of Patent Monopoly for Marketed Drugs via Operation of Linkage Regulations.**  
*a.* Period of extended patent protection for averaged drugs in the subset ( $n=16$ ). Left and right sigmoid curves represent cumulative patent protection start and end dates. The term of patent protection was deemed to begin on the priority date. Terms are shown for the “originating patent” on the New Active Substance/New Chemical Entity (●;  $n=1$ ) and all “subsequent patents” (●;  $n=21$ ). The date on which patents were listed on the register is also shown (◆;  $n=4$ ). The duration of theoretical and actual patent protection under linkage regulations associated with originating and subsequent patents are illustrated by representative horizontal lines and shading along the time axis. Note the period of patent protection associated with originating patents lasted about 20 years (■), from 1983 to 2003. In comparison, the duration of extended patent protection associated with all subsequent patents was much longer (~two-fold; ■), lasting from about 1987 to 2028. Of the forty-eight patents granted per drug, an average of five were listed on the patent register. The term of protection associated with these patents ran from 1993 to 2025 (■). This yielded an actual extended period of patent protection of twenty-two years beyond that afforded by the originating patent. Note that due to strategic listing of patents on the patent register (◆), there was little difference between theoretical and actual patent protection under linkage regulations. Reproduced courtesy of the *Berkeley Technology Law Journal*.<sup>6</sup>

As shown in Fig. 6, of the 772 patents on sixteen products, 5% were listed on the patent register. While 5% may seem a small figure at first blush, when analyzed the data revealed that strategic listing of only a handful patents on the patent register yielded a cumulative patent term that was nearly equivalent to that of all forty-eight patents granted. An ancillary observation is that this term is only five years less than the term of patent protection under circumstances where all forty-eight patents on the group are added up and *not legally contested at all*, as listing a patent is not the same as litigating it.

We also provided data in Study 3 on a single drug, Omeprazole, for which patenting and patent listing patterns dovetailed well with results

from the averaged data. Litigation data on this drug revealed an astounding number of trials, motions, appeals, and decisions at the same level of court with differing results. We identified eighty-two patents associated with two drug forms of Omeprazole, Losec<sup>®</sup> and Nexium<sup>®</sup>, that were granted over a period of twenty years. The patents had a cumulative term of patent protection of close to fifty years. The priority dates for the first and final patent were 1978 and 2005, respectively. Therefore, the period of hypothetical patent protection on the Omeprazole group ran from 1975 to about 2025. In comparison, the first NOC for Omeprazole (Losec<sup>®</sup>) was granted on June 13, 1989, yielding a regulatory gap of close to ten years. Of eighty-two patents that were deemed relevant to Omeprazole, 27% (n=22) were listed on the patent register. Compared to the average of 5% on the group, the data indicate that once the market vets a compound as “high value,” firms increase patent listing.

At the completion of our analysis (December 31, 2008), there were 61 separate trials on twenty-two listed patents, including 310 motions (mean=5.08 per trial) and twenty-five final trial decisions. Of final decisions, fourteen went on to appeal at the Federal Court of Appeal and eight went on to the Supreme Court of Canada. Litigation occurred over a term of sixteen years, essentially from the time the linkage regulations came into force in 1993 until the present. Four trials on twelve patents are currently ongoing. The average date on which relevant trials ended, and thus, the date of “reactivation” of the average generic approval was December 2003.

Under the terms of the NOC Regulations, litigation over patents relating to Losec<sup>®</sup> and Nexium<sup>®</sup> resulted in a delay of market entry of close to three (2.83) years for the group. According to IMS Health,<sup>27</sup> sales of the two drugs in drugstores and hospitals over the same time frame were CN \$1.4 billion. In comparison, total spending on prescription pharmaceuticals rose from CN \$11.7 billion in 2001 to CN

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27. INTERCONTINENTAL MKTG. SERVS. HEALTH INC., 2003 ANNUAL REPORT TO SHAREHOLDERS (2003), *available at* <http://www.imshealth.com/portal/site/imshealth>; INTERCONTINENTAL MKTG. SERVS. HEALTH INC., 2002 ANNUAL REPORT TO SHAREHOLDERS (2002), [http://media.corporate-ir.net/media\\_files/NYS/RX/reports/-ar2002.pdf](http://media.corporate-ir.net/media_files/NYS/RX/reports/-ar2002.pdf); INTERCONTINENTAL MKTG. SERVS. HEALTH INC., 2001 ANNUAL REPORT TO SHAREHOLDERS (2001), *available at* <http://www.imshealth.com/portal/site/imshealth>. *See also* INTERCONTINENTAL MKTG. SERVS. HEALTH INC., CANADIAN PHARMACEUTICAL INDUSTRY REVIEW (2001) (on file with author); INTERCONTINENTAL MKTG. SERVS. HEALTH INC., CANADIAN PHARMACEUTICAL INDUSTRY REVIEW (2002) (on file with author); INTERCONTINENTAL MKTG. SERVS. HEALTH INC., CANADIAN PHARMACEUTICAL INDUSTRY REVIEW (2003) (on file with author).



\$17.97 billion in 2004,<sup>28</sup> representing an increase of 92%. This includes an increase in out-of-pocket consumer spending from CN \$2.56 billion to CN \$3.36 billion.

Data pertaining to Ompeprazole and other blockbuster drugs subject to heavy litigation at the same time require updating, as amendments to linkage laws have been made over the last three to four years that have narrowed the scope of listed patents to those specific to a given submission and that prevent multiple automatic injunctions per reference product. Having said this, our newer data provide multiple examples of similar “product clusters” enabled by linkage, a theory for which is explored in Section III.A. below. It is reasonable to speculate however that “but for” the existence of the linkage regime that generic entry may have occurred closer to expiry of the originating patent or patents, as anticipated by the government prior to the NOC Regulations coming into force,<sup>29</sup> with an accordingly shorter period of delayed entry. Either way, the linkage regime has proved to be a highly effective mechanism for extending market monopolies on profitable drugs.

#### *D. Interpretation*

A linkage regime that provides patent protection on poorly innovative drugs that extends well beyond the term of originating patents, not only has the potential to debilitate the patent system in the short term, but also to weaken pharmaceutical innovation more generally in the long term.<sup>30</sup> In the context of the linkage regime, the weak relevance requirement acts in combination with the automatic injunction and low evidentiary requirements for new and follow-on drug approval to yield a situation where the notion of patent protection can be taken to a point near its logical extreme. The data reviewed above suggest that if linkage regimes provide fertile grounds for firms to compete at a lower level of innovation, they also discourage firms from innovating at a level of competition that would provide the greatest benefit to society. This dilemma can be illustrated by a comparison of the data from Studies 1 and 3.

On the one hand, it was demonstrated that a very small fraction of drugs approved by regulators over the eight-year test period could be

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28. CAN. INST. FOR HEALTH INFO., *DRUG EXPENDITURE IN CANADA, 1985 TO 2008*, at 6, 60 (2009).

29. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:37–40 (Dec. 1, 1992) (testimony of Minister Michael Wilson and Dr. Elizabeth Dickerson).

30. *Graham v. John Deere Co.*, 383 U.S. 1, 17–18 (1966); *Whirlpool Corp. v. Camco, Inc.*, [2000] 2 S.C.R. 1067, ¶ 37 (Can.).

considered truly breakthrough in nature based on several metrics. This includes drugs approved via the NDS stream (16%), those containing a NAS (6.1%), total drugs (NDS and SNDS) directed to First in Class therapies (6.5%), those that underwent one of two pathways (priority review; NOC/c) for expedited review (5.3%), and those that met the most stringent requirements for breakthrough products (1.23%; 1.87% of brand-name approvals).

On the other hand, the linkage study illustrated that patent protection under linkage regulations does not discriminate between poorly or strongly innovative drugs. It arbitrarily offers to pharmaceutical firms broad and long-lasting intellectual property rights targets, regardless of the types of products being introduced into the marketplace. This is a particularly relevant point for follow-on drug products, which are well recognized to entail lower risks and costs to pharmaceutical firms,<sup>31</sup> yet which also are associated with an enhanced term of monopoly pricing. As suggested by the data from Study 1, the evolution toward a lifecycle-based regulatory approach to drug approval will likely do little to affect the rate and direction of innovative activity by firms absent shifts in legal incentives for breakthrough and follow-on drug development.

Discordance between the basket of patent rights incentives for innovation and resulting product development is further supported by data from Study 3. For example, the close temporal relationship between drug approval and patent listing and the strong convergence of patent grants and patent listing following the coming into force of linkage regulations provides evidence for the conclusion that patent listing evolved into a more effective target, and thus, a better proxy, for drug approval than drug patenting per se once the linkage regime came into effect. Other evidence for this conclusion comes from data showing that steep time-dependent changes in drug patenting, patent listing, and the evolution toward lifecycle regulation appeared to have occurred independently of concomitant trends for new and follow-on drug approvals.

The outcome of this dynamic, supported by averaged data for sixteen drugs and the single example of Omeprazole, is that pharmaceutical firms can leverage government policy and regulation where given the opportunity to maintain market share for drugs coming off patent rather than developing new blockbuster drugs. The results are not dissimilar to studies of complex political systems, where “yardsticks” designed to measure progress reorient behavior narrowly

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31. Cohen 2005, *supra* note 22, at 78.

towards fulfillment of yardstick metrics.<sup>32</sup>

Our analysis of the drug approval-patenting linkage shows that new drug development has stagnated while follow-on drug development has flourished since the NOC Regulations came into force. However, as illustrated by the results in Study 2, these trends have been accompanied by increasing and faster utilization of both established patent law and emerging linkage regulations by pharmaceutical firms. Moreover, the large array of patent and therapeutic classifications indicated that firms are focused on expanding the ever-widening pool of patents for purposes of both follow-on drugs and for patent listing purposes. The data also support a focus by firms on a “paradoxical drug approval-patent linkage,” whereby firms receive the largest scope of intellectual property protection for the lowest level of innovation.

The data in Studies 1, 2, and 3 indicate that in combination the existing framework for drug approval, the traditional patent system, and the emerging linkage paradigm has afforded the largest scope of intellectual property protection to pharmaceutical products in the history of Canada. The implication of the results as a whole is that firms are aiming *ex ante* at legal targets that provide the most return on investment rather than innovative products providing the most benefit to the public.

An important aspect of the work described above is that it provides objective evidence demonstrating that even though many follow-on drugs have little or no therapeutic value over existing products, they can nevertheless be used to powerfully extend market exclusivity for blockbuster drugs. Patents on such products can be used for this purpose either by providing the basis for follow-on drug submissions or by providing a large pool for patenting listing purposes. In either case, breakthrough innovation is diminished at the same time as the timely entry of generic products is delayed.

Finally, empirical data such as those reviewed above have implications for innovation theory in general, which often posits that incremental or follow-on innovation is just as important to overall innovation as pioneering innovations. Indeed, the pharmaceutical industry has been consistently heralded as the best example of the success of the patenting regime, almost in the complete absence of objective empirical data.<sup>33</sup> In this regard, it is noteworthy that because

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32. ROBERT JERVIS, SYSTEM EFFECTS: COMPLEXITY IN POLITICAL AND SOCIAL LIFE 87 (1997) (noting that “the interactions in the system may alter the meaning of the yardstick.”).

33. BOLDRIN & LEVINE, *supra* note 9, at 212.

of weak regulatory requirements for new and follow-on drug approval and for patent listing, follow-on drugs that may have little or no therapeutic benefit compared to existing drug products can be used to substantially extend market exclusivity on blockbuster drugs that do have significant benefits to the public at large.<sup>34</sup> Thus, the social consequences of a *regulatory preference* for follow-on drugs may be greater in the public health sector than other sectors of the economy. This issue is explored more fully in Section III.A. below in terms of product clusters.

## II. ARE THE REGULATIONS A SUCCESS?

This section of the Article provides a discussion of the performance of the linkage regime in light of the empirical data reported above and the stated policy goals underpinning the NOC Regulations to stimulate the development of new and innovative drugs and facilitate timely market entry of generic drugs.

One of the major promises made by the U.S. pharmaceutical industry in the lead-up to both Bill C-22 and Bill C-91,<sup>35</sup> supported by domestic universities, was to inject billions of dollars into domestic research and development activities. This investment was specifically targeted towards the production of innovative therapeutic products. The Minister of Industry, Science and Technology, Michael Wilson, along with the Minister of Consumer and Corporate Affairs, Michael Blais, both equated intellectual property rights with pharmaceutical innovation and hailed the new regime as the beginnings of a new, more innovative nation.<sup>36</sup> Mr. Wilson went further, declaring that the injection of millions of dollars into domestic research and development would enable Canada to transition into “a world-class pharmaceutical industry. . . .”<sup>37</sup> Claims of this nature were made at the same time as government was receiving evidence to the effect that amendments to its domestic patent laws would chill generic competition, cost Canadian consumers between CN \$4 and \$7 billion over a fifteen-year period,<sup>38</sup> and that the CN \$500 million in research and development investment

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34. See *infra* notes 61 and 62 and accompanying text for detailed discussion of the therapeutic value of follow-on drugs.

35. Harrison, *supra* note 4, at 491.

36. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:39–42 (Dec. 1, 1992).

37. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:30 (Dec. 1, 1992).

38. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:68–92 (Dec. 1, 1992).

by multinational firms was actually composed in large part of substantial tax incentives ranging from 50% to 70%, depending on the province.<sup>39</sup>

Experience since the dates on which pharmaceutical linkage came into force in the United States and Canada has shown that the legal definitions of “research” and “development” costs are very controversial,<sup>40</sup> with industry critics claiming that marketing, advertising, opportunity and other related costs are in fact driving this line item.<sup>41</sup> There is ample evidence demonstrating that the pharmaceutical industry will take whatever steps necessary to protect what it sees as confidential

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39. For a review of the evidence in front of the House of Commons in the context of Bills C-22 and C-91, see Harrison, *supra* note 4, at 511–524 and Jordan, *supra* note 3. In the Parliamentary debate leading up to enactment of Bill C-91, it was widely noted by several Members of Parliament that the CN \$300–500 million figure had to be reduced in accordance with provincial tax incentives, which amounted to fifty-five, sixty, and seventy cents on the dollar in Alberta, Ontario, and Quebec, respectively, *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:4 Parliament of Canada, 4:14, 4:39 (Nov. 27, 1992) and *id.* at 34:5 Parliament of Canada, 5:38, 5:40, 5:91 (Nov. 30, 1992). During cross-examination, federal employees acknowledged that these figures were correct and that the calculations were intentionally left out of government reports on topic leading to the hearings. *Id.* at 34:6 Parliament of Canada 6:10 (Nov. 30, 1992).

40. For a detailed history of litigation over public disclosure of pharmaceutical R&D costs, see generally U.S. CONG. OFF. OF TECH. ASSESSMENT, PHARMACEUTICAL R&D: COSTS, RISKS, AND REWARDS 284•88 (1993) [hereinafter OFF. OF TECH ASSESSMENT]. The U.S. Supreme Court, in the seminal *Bowsher v. Merck Co.* decision, held that pharmaceutical R&D and related costs, constituted confidential information and, thus, that the federal government did not have the authority to compel disclosure of such information. 460 U.S. 824, 843 (1983). For a more recent discussion of pharmaceutical R&D costs see U.S. NAT'L INST. OF HEALTH, NIH RESPONSE TO CONFERENCE REPORT REQUEST FOR PLAN TO ENSURE TAXPAYER'S INTERESTS ARE PROTECTED (2001), available at <http://www.nih.gov/news/070101wyden.htm>. In Canada, data submitted by pharmaceutical companies are deemed to be “commercially sensitive” and as such constitute confidential information under the Federal Access to Information Act. See R.S.C., 1985 c. A-1 20(6). Under Section 20(6), disclosure can only be made where it is in the public interest and relates to public health and safety. *Id.* Health Canada will not, however, release information where public interest in disclosure is outweighed by financial loss or prejudice to the competitive position of the disclosing party. *Id.* See also NAFTA, *supra* note 2, at art. 1711; TRIPS, *supra* note 2, at art. 39 (pertaining to data and market exclusivity, which deem commercially sensitive information to be confidential). See generally Regulatory Impact Analysis Statement, 138 C. Gaz. pt. I, at 3712 n.50 (2004). (Regulations Amending the Food and Drug Regulations [1390 - Data Protection]), as modified by Regulatory Impact Analysis Statement, 140 C. Gaz. pt. I, at 1598 n.24 (2006) (Regulations Amending the Food and Drug Regulations (Data Protection)).

41. See *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:4 Parliament of Canada, 4:12, 4:20 (Nov. 27, 1992) (testimony of the Canadian Medical Association) and *id.* at 34:7 Parliament of Canada, 7A:51 (Dec. 1, 1992) (testimony from Green Shield). For a discussion of the role of marketing generally in Canada, see Trudo Lemmens & Ron A. Bouchard, *Regulation of Pharmaceuticals in Canada*, CANADIAN HEALTH L. AND POL'Y 311, 312 (3d ed. 2007).

information relating to research and development expenditures,<sup>42</sup> even when the U.S. Government Accountability Office is doing the asking.<sup>43</sup> In light of uncertainties as to how much financial support foreign firms have, in fact, provided to domestic research and development activities, the remaining discussion focuses on the data we do have in hand; that is, whether drugs approved following enactment of the NOC Regulations constitute new or follow-on drugs and the degree to which the legal link between drug approval and drug patenting under the NOC Regulations has provided for extended intellectual property protection that would not have occurred 'but for' operation of the linkage regime.

The following section provides a brief historical overview of portions of the debate leading up to the enactment of the linkage regime, discussion of the original policy intent underpinning the regulations according to the federal government, a review of selected Supreme Court of Canada jurisprudence and principles of statutory interpretation that may be instructive when interpreting the broad purpose of the linkage regime, and finally, a reinterpretation of the empirical data in Studies 1, 2, and 3 based on the above material.

#### *A. Debate Preceding Bill C-91*

As well described in the literature and case law, compulsory licensing of pharmaceuticals was introduced in Canada in 1923 and expanded yet again in 1969 to control increasing drug costs. In 1987, amendments to the Patent Act in the form of Bill C-22 limited compulsory licensing and created the Patented Medicine Prices Review Board (PMPRB) to ensure that the prices of patented pharmaceuticals were not excessive. The second, and more major, round of reforms came in 1993, at which time Bill C-91<sup>44</sup> eliminated compulsory licensing, harmonized patent protection of pharmaceuticals in Canada with other developed nations, and enacted the Patented Medicines (Notice of Compliance) Regulations. Not surprisingly, many of the issues subject to intense criticism and judicial review since then were raised in the limited period of examination of Bill C-91, during the end of the 34th Session of Parliament in December 1992. These issues include: the impact of the bill on drug costs, domestic research and development investments, patent terms, job creation, and the trickle-down effects of

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42. Thomas O. McGarity & Sidney A. Shapiro, *The Trade Secret Status of Health and Safety Testing Information: Reforming Agency Disclosure Policies*, 93 HARV. L. REV. 837 (1980); Jeffery M. Drazen, *Who Owns the Data in a Clinical Trial?*, 8 SCI. ENG. ETHICS 407 (2002).

43. OFF. OF TECH. ASSESSMENT, *supra* note 40.

44. The Patent Act Amendment Act, S.C. 1992, c. 2 (Can.).

increased public health costs. However, with one major exception, the debate was characterized by a significant lack of foresight about the extent to which the reforms would impact patent protection for pharmaceuticals and the regulatory mechanisms through which this change would be effected.

One of the primary points of contention in the Bill C-91 debate was investment of money by foreign multinationals into domestic research and development activities and the translation of this support into new and innovative products. The Minister of Industry, Science and Technology, the Minister of Consumer and Corporate Affairs, and almost all of the major provincial universities equated increased intellectual property protection with increased research, increased innovation, and increased national productivity.<sup>45</sup> In particular, extended patent rights were seen as the gateway to enhanced production of new and innovative technologies that could compete globally. Support of expanded patent protection by industry and government sectors is well known. Less known, however, was the role of the Canadian university system in this process. University advocates, including those with clear conflicts of interest, claimed that industry profits resulting from enhanced patent protection would create a better society for Canadians.<sup>46</sup> It was simply assumed by university advocates that increased intellectual property protection was positively related to increased innovation and increased therapeutic benefit to the public.

This sentiment was not unanimous among Legislative Committee members or witnesses appearing before the Committee. In particular, the Committee heard evidence from at least two major reports to the contrary that bear further scrutiny. A 1981 OECD study<sup>47</sup> noted that when governments with historically low levels of pharmaceutical

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45. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:8, 5:114, 5:116 (Nov. 30, 1992) and *id.* at 34:8 Parliament of Canada, 8:24, 8:28 (Dec. 1, 1992) (testimony of Tyrell, UT, Group of 10, Minister Blais, and Minister Wilson).

46. *See, e.g., Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:20 (Nov. 30, 1992) (testimony of Lorne Tyrrell, who himself was the recipient of substantial pharmaceutical funding, which helped to create a spin-out company from which he personally profited). The notion that pharmaceutical funds were "vital" to the health of Canadian universities was supported by testimony from other university administrators, including the so-called "group of 10." *See, e.g., id.* at 34:5 Parliament of Canada, 5:116.

47. M.L. Burstall, J.H. Dunning, & A. Lake, *Multinational Enterprises, Governments and Technology—the Pharmaceutical Industry*, (Paris: OECD, 1981) (cited in the Canadian Health Coalition and Medical Reform Group Brief, *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5A:73, A5:83 (Nov. 30, 1992)).

research and development try to stimulate it through policy levers such as patent rights, the results have been disappointing. The Eastman Commission<sup>48</sup> similarly noted that Canada lacks the fundamental resources to be a global force in pharmaceutical research and development. The Commission went further, stating that providing multinational firms with enhanced domestic patent rights would not increase domestic innovation, given long established research and development centers elsewhere.<sup>49</sup> As argued by one Committee member,<sup>50</sup> conclusions such as those of Eastman and the OECD were consistent with data from a federal study showing Bill C-22 had minimal impact on university research and development activity. Nevertheless, the Minister of Consumer and Corporate Affairs, Harvie Andre, in the lead up to Bill C-22, and Michael Wilson, the Minister of Industry, Science and Technology at the time Bill C-91 was debated, continued to assert that increased patent rights would enable Canada to innovate on a “world scale” and to develop a “world-class pharmaceutical industry . . .”<sup>51</sup>

A point that resonates particularly well with the data reported in Study 1 also was raised by the Canadian Association of Consumers (CAC). The CAC expressed concern that patent reforms providing greater protection for Me Too and Line Extension drugs would come at the cost of truly innovative drugs and innovative health research generally. Citing the Eastman report, the CAC noted that patent rights are not inalienable and are granted by governments cautiously *with the specific purpose* of stimulating an “appropriate amount of innovation.”<sup>52</sup> However, the issue of including definitions of the desired level of

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48. REPORT OF THE COMMISSION OF INQUIRY ON THE PHARMACEUTICAL INDUSTRY. (Supply and Services Canada 1985) (cited in *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:12 (Nov. 30, 1992)).

49. This point was also raised by the Canadian Consumer Protection Agency in its submissions (cited in *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:41 (Nov. 30, 1992)).

50. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:12 (Nov. 30, 1992) (Testimony of Mr. MacDonald (Dartmouth) (citing a Canadian Industry, Science and Technology Report, entitled “Impact of Pharmaceutical Company Sponsored Research on Basic Research in Canadian Universities.”)).

51. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:30 (Dec. 1, 1992) (Testimony of Minister Wilson); *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5A:73, 5A:81 (Nov. 30, 1992) (CHC Brief).

52. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:60, 5A:19, 5A:20, 5A:30 (Nov. 30, 1992) (Canadian Association of Consumers, submissions and brief).



innovation resulting from increased patent rights or even evidence-based output metrics for research and development investments was not taken up by many in the debate despite repeated calls for such outcomes by some participants in the hearings.<sup>53</sup>

Insightful comments were also made by the CAC on the potential ramifications of extended patent protection for the development of new and innovative drugs.<sup>54</sup> Milton Friedman was cited to the effect that patent monopolies too often provide strong incentives to shift research and development towards products like Me Too drugs where patents are more easily granted. The key observation being that, as with patents granted by the Patent & Trademark Office,<sup>55</sup> drug regulators are in the routine and predictable habit of granting approvals on products with low innovative value. As used here, the phrase “low innovative value” refers to follow-on drugs that have little or no therapeutic benefit over existing marketed drugs.

Indeed, the Committee heard evidence from an Industry, Science and Technology study before the Committee<sup>56</sup> that indicated that 80% of clinical practitioners deemed domestic research and development to be in service of Me Too drugs. This observation accords with our data

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53. Both the Canadian Medical Association (CMA) and Canadian Association of Consumers (CAC) requested that the federal government take an “evidence-based” approach to assessing research and development costs and the impact of patent reforms on the costs and benefits of the public health system. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:53 (Nov. 30, 1992) (CAC); *id.* at 34:4 Parliament of Canada, 4:8, 4A:18, 4:10 (Nov. 27, 1992) (CMA); Harrison, *supra* note 4, at 526 (concluding in his study of the political and economic factors underpinning Bill C-22 and Bill C-91 that “one cannot persuasively argue that the Mulroney administration tied or linked this costly policy (repeal of compulsory licensing) to any tangible benefit.”). Indeed, during the debate over repeal of compulsory licensing and patent reforms in the lead up to TRIPS, NAFTA, and Bill C-22, proponents of increased patent protection were criticized for the lack of commitments by the pharmaceutical industry that would be “measureable and enforceable.” *Id.* The Minister of Consumer and Corporate Affairs at the time, Harvie Andre, replied that output metrics were not necessary, saying instead “[w]e prefer carrots to whips. If it turns out that the donkey will not go with the carrot then maybe you will have to use the whip.” *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-22*, 33:2 Parliament of Canada, 1:11, 1545 (December 16, 1982) (cited in Jordan, *supra* note 3, at 31–32).

54. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5A:30 (Nov. 30, 1992).

55. Mark A. Lemley, *Rational Ignorance at the Patent Office*, 95 NW. U. L. REV. 1495, 1495 (2001).

56. CHC Brief, *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5A:72, 5A:83 (Nov. 30, 1992). (citing K.M. Taylor, *The Impact of the Pharmaceutical Industry’s Clinical Research Programs on Medical Education, Practice and Researchers in Canada: a Discussion Paper*, in CANADIAN PHARMACEUTICAL RESEARCH AND DEVELOPMENT: FOUR SHORT-TERM STUDIES (Dept. of Industry, Science and Technology, Ottawa 1991)).

that nearly 60% of all drugs approved by Canadian regulators between 2001 and 2008 were Me Too drugs.<sup>57</sup> It is also consistent with statements made by the Medical Directors at Pfizer and Squibb that as much as 75% of scientific research had been channeled into “copycat drugs and unimportant combinations.”<sup>58</sup> Even Dr. Eastman, while providing testimony before the Committee as Chair of the PMPRB, acknowledged that there is little therapeutic benefit to be gained from Me Too and, particularly, Line Extension drugs.<sup>59</sup> This statement accords with the results of later studies conducted in Canada, France, and the United States,<sup>60</sup> including those in Studies 1, 2 and 3. Finally, the Committee heard testimony about the “natural experiment” in Italy, where de novo institution of patent protections that were harmonious with those in the United States actually reduced national innovation and drove up the costs of drugs.<sup>61</sup> Acknowledging room for debate in the interpretation of these studies, it is nevertheless clear that at the time the linkage regime came into force, there was significant evidence to suggest that increased patent rights would lead to neither enhanced innovation nor timely generic entry.

In retrospect, perhaps the most remarkable aspect of the debate leading up to the passage of Bill C-91 was that Section 4 of the Patent Act Amendment Act containing the linkage regulations was hardly debated at all, let alone noticed by most participants at the hearings. The original goal of the amendments was to allay concerns by brand-name drug manufacturers that generic firms might use the provisions of the legislation allowing generics to seek regulatory approval without being subject to infringement (the so-called “early working” exception) to sell these products before the patent expired.

Misunderstandings of the purpose, procedures, and even existence of the linkage regulations were widespread. For example, the

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57. Bouchard 2009, *supra* note 14, at 1491.

58. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:20 (Dec. 1, 1992).

59. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:46 (Dec. 1, 1992).

60. PATENTED MEDICINE PRICES REVIEW BOARD, ANNUAL REPORT 2000, 24 (2001); *Bogus Innovation*, *supra* note 21; *Drugs in 2001*, *supra* note 21; Kenneth I. Kaitin, *supra* note 21; Joel Lexchin, *Intellectual Property Rights and the Canadian Pharmaceutical Marketplace: Where Do We Go From Here?*, 35 INT'L. J. HEALTH SERVS. 237, 243 (2005); Domenico Motola, *supra* note 21; PHARMACEUTICAL INNOVATION, *supra* note 21 at 7; and *New Medicines in 2007*, *supra* note 21.

61. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:134 (Nov. 30, 1992) (Canadian Health Coalition); *id.* at 34:7 Parliament of Canada, 7:13 (members of Parliament) (Dec. 1, 1992).

Committee heard testimony that only sixteen drugs would be affected by the regulations.<sup>62</sup> Several policy makers called as witnesses claimed they were not sure even why they were called to the proceedings,<sup>63</sup> stating on a number of occasions<sup>64</sup> that they lacked the qualifications to comment on Bill C-91 even though they were responsible for drafting related policy documents based on which more senior officials were testifying. Also common was the assertion that drugs that would be affected by the legislation were only associated with one patent, and thus, it was only one patent extension that generics had to contend with when waiting for market entry. The most significant comments of this nature came from Dr. Elizabeth Dickson, Director General, Chemical and Bio-Industries Branch, Department of Industry, Science and Technology. Dr. Dickson testified that, "I must explain that when a new medicine comes on the market there is a *main patent*. When *that main patent expires*, anyone may copy that product and bring it to market."<sup>65</sup>

The general consensus at the hearings, included in testimony from the Canadian Health Collation,<sup>66</sup> Dr. Dickson,<sup>67</sup> and Michael Wilson, Minister of Industry, Science and Technology,<sup>68</sup> was that patent reforms pursuant to Bill C-91 would increase market exclusivity for brand-name pharmaceuticals by only one to three years.

The lone voice of dissent was Dr. Stephen Schondelmeyer, a U.S. economist and pharmacologist who conducted an independent study on the potential impact of Bill C-91. It is not surprising an American would bring the most experienced voice to the table. Indeed, it is obvious from the language, concepts, and even the measurements he employed in his

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62. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:126 (Nov. 30, 1992) (comment made by a Vice President of Research from UBC).

63. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:6 Parliament of Canada, 6:4 (Nov. 30, 1992) (Mr. David Blaker, Head, Risk Assessment and Management Section, Bureau of Drug Research, of National Health and Welfare).

64. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:6 Parliament of Canada, 6:6-7, 6:9-11 (Nov. 30, 1992) (Mr. Blaker). Another witness, Mr. Ross Duncan (Consumer Policy Branch, Department of Consumer and Corporate Affairs), testified that the only data he used to construct his report on the impact of Bill C-91 was data provided by the Pharmaceutical Manufacturers Association of Canada (PMAC). *Id.* at 6:12.

65. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:37 (Dec. 1, 1992) (emphasis added).

66. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:76; 5:133 (Nov. 30, 1992).

67. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:40 (Dec. 1, 1992).

68. *Id.*

analysis that Dr. Schondelmeyer had several years of experience with the U.S. Hatch-Waxman linkage regime prior to giving testimony relating to Bill C-91. In addition to predictions based on empirical data, the most important contribution made to the debate was introducing for the first time a focus on cumulative market exclusivity rather than on patent term per se:

In fact, you may not realize that most pharmaceutical products have two, three, or even four patents that protect them, not just one patent. They'll have a patent on the chemical entity itself. There'll be a patent on the dosage form. There'll be a patent on the use of the product in some cases, and sometimes a patent on the process by which the pharmaceutical is made. *So one can't analyse [sic] the impact of this patent extension simply by looking at the extension of an individual patent. What you have to analyse [sic] is the effect of the combination of those patents that are extended and how much that extends the total market exclusivity of a given pharmaceutical.*<sup>69</sup>

Based on his study, Dr. Schondelmeyer suggested that, in sharp contrast to the three years of market extension alluded to above, 33% of products affected by Bill C-91 would have increased market exclusivity by a term of ten years or more.<sup>70</sup> Moreover, due to increasingly harmful effects on innovation, the short-term effects would be far less onerous than the long-term effects, with the worst impact on innovation and extended market exclusivity being seen about ten years after Bill C-91 came into force.<sup>71</sup> As discussed in more detail below, this is consistent with our data from Studies 1 and 3 showing steadily declining new drug development, steadily increasing follow-on innovation, steadily increasing patent protection over the last decade accompanied by increasing delays for generic entry. As noted above, Dr. Dickson and Michael Wilson vigorously denied the importance of cumulative market exclusivity, maintaining that only one patent per drug prevented generic entry and that Bill C-91 would only increase exclusivity by a maximum of three years.

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69. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:68 (Dec. 1, 1992) (emphasis added).

70. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:68, 7A:111 (Dec. 1, 1992).

71. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:70 (Dec. 1, 1992). (Professor Schondelmeyer assessed the net cumulative savings to Canadians (individual consumers, hospitals and insurance plans) from 1993 to 2010 would be CN \$7 billion in constant 1993 dollars).

In addition to the strength of the U.S. pharmaceutical lobby,<sup>72</sup> trade harmonization efforts in the context of GATT<sup>73</sup> and NAFTA,<sup>74</sup> pressures from Quebec politicians and lobbyists,<sup>75</sup> and concerns about incoming then-President-Elect Bill Clinton perhaps looking to a system of price control for pharmaceuticals not unlike that of the PMPRB,<sup>76</sup> another reason for the patent reforms of Bill C-22 and C-91 was provided by the CAC. In its testimony before the Parliamentary Committee on Bill C-91,<sup>77</sup> the group claimed that patent reforms such as those enshrined in Bill C-22 and Bill C-91 represented a naïve effort by the federal government to attract research and development funds in competition with other global jurisdictions with more established research and development bases that were using their patent systems and tax bases in the same way. The CAC claimed that leveraging intellectual property strategy in this manner could not reasonably result in positive social welfare outcomes. Rather, the more likely result was that reforms of this nature would induce a flow of capital to nations who have taxpayers with the deepest pockets.<sup>78</sup> Instead of stimulating innovation, or even

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72. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:42 (Nov. 30, 1992) (Canadian Centre for Policy Alternatives (CCPA)). The pharmaceutical industry was reportedly the second largest contributor to U.S. election campaign funding. See, e.g., *How Health PACs Spend Millions to Influence Elections*, Washington Post, Mar. 21, 1989, at 14 (cited in 34:7 Parliament of Canada, 7A:45 (Dec. 1, 1992)).

73. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:42 (Nov. 30, 1992) (CCPA).

74. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:49 (Nov. 30, 1992).

75. For a first-hand view, see all nine volumes of *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34 Parliament of Canada (1992). For an arm's length view, see generally Harrison, *supra* note 4; Tancer, *supra* note 4.

76. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:73 (Nov. 30, 1992); *id.* at 34:7 Parliament of Canada, 7:18 (Karpoff), 7:99 (Canadian Drug Manufacturers Association (CDMA)) (Dec. 1, 1992). *But see id.* at 34:8 Parliament of Canada, 8:37 (Dec. 1, 1992) (Minister Wilson, for a strong rebuttal of this argument). For a historical discussion of why President Clinton might support price controls in the United States while seeking intellectual property privileges globally, see Harrison, *supra* note 4, at 461, 522, 523, 526.

77. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:54–57 (Nov. 30, 1992).

78. As a reminder, between fifty and seventy percent of the proposed sum of CN \$500 million that the pharmaceutical industry would invest in domestic research and development was composed of provincial tax breaks. This is particularly relevant given testimony by Dr. Joel Lexchin before the C-91 Committee, *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:5 Parliament of Canada, 5:135 (Nov. 30, 1992) that the majority of profits for provincial drug plans are due to savings from generic drugs. In addition to provincial tax savings, Canada is known to have one of the more generous Scientific Research and Experimental Development (SRED) tax credit programs. *Id.*

providing incentives for innovation, the net result is capital market protectionism by multinational pharmaceutical firms. It is here where the “paradoxical drug approval-drug patenting linkage” described in our Northwestern study<sup>79</sup> is particularly relevant, as the evidence we obtained suggests that firms may be strongly targeting their drug development efforts towards products with the greatest patent protection and the least amount of innovation.

A related point, which accords well with later developed models of policy resistance<sup>80</sup> and policy failure<sup>81</sup> is the apparent failure of both legislators and policy-makers to at least anticipate some of the unintended consequences and feedback loops of rapidly pushing through widespread patent reforms based on a hitherto unexplored link between the goals and objects of industrial patent law with those of food and drug law:

[A]s one involved in public policy, often the decisions we make quickly and without thorough evaluation are decisions that come back to haunt us. Most legislation is precipitated by some critical event that has occurred. We try to quickly develop legislation that responds to that critical event and then often find out after the fact that in addition to trying to solve the initial problem we have created a number of unintended consequences down the line that we have to go back and fix and correct.<sup>82</sup>

### B. “Original Policy Intent”

Often courts are left without clear guidance by government, either before or after legislation or regulations come into force. Fortunately, the specific policy grounds underpinning the NOC Regulations have been articulated by the federal government in numerous government Regulatory Impact Analysis Statements (RIASs).<sup>83</sup> The Supreme Court

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79. See *supra* Section III.

80. See generally John D. Sterman, *All Models Are Wrong: Reflections on Becoming a Systems Scientist*, 18 SYS. DYNAMICS REV. 501 n.4 (2002).

81. See generally Barry Bozeman & Daniel Sarewitz, *Public Values and Public Failure in US [sic] Science Policy*, 32 SCI. AND PUB. POL’Y 119 n.2 (2005); Barry Bozeman, *Public-Value Failure: When Efficient Markets May Not Do*, 62 PUB. ADMIN. REV. 145, 145 (2002).

82. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:92 (Dec. 1, 1992).

83. Evidence of legislative intent regarding balancing patent enforcement and generic entry can be found in early RIAS documents. See 138 C. Gaz. 50 Pt. I, 3714 (2004); 140 C. Gaz. 24 Pt. I, 1601 (2006); 142 C. Gaz. 13 Pt. II, 1390, 1588 (2008); Health Can., Health Prods. & Food Branch, Guidance Document, Patented Medicines (Notice of Compliance) Regulations (2010), [http://www.hc-sc.gc.ca/dhp-mps/alt\\_formats/hpfb-dgpsa/pdf/prodpharma/applic-demande/guide-](http://www.hc-sc.gc.ca/dhp-mps/alt_formats/hpfb-dgpsa/pdf/prodpharma/applic-demande/guide-)

of Canada has ruled that such documents constitute proper evidence of legislative intent, including in the context of litigation under the regulations.<sup>84</sup>

According to a series of RIAS documents over a period of approximately ten years, the “original policy intent” in enacting the linkage regime was to balance patent enforcement *over new and innovative drugs* with the *timely* market entry of generic drugs. The two pillars of the regulations were to increase production of new and innovative drugs while getting older drugs genericized as quickly as possible. Importantly, the NOC Regulations were intended to operate in accordance with the established principles of patent law,<sup>85</sup> and to further the “societal imperative” of developing new remedies to enhance public health.<sup>86</sup> The specific linkage between the goals and objectives of food and drug law with those of patent law is said to reaffirm the “stability, predictability and competitiveness of Canada’s pharmaceutical patent regime”,<sup>87</sup> a link vetted by multinational pharmaceutical firms themselves before and after the Canadian linkage

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ld/postnoc\_change\_apresac/noc\_pn\_framework\_ac\_sa\_cadre-eng.pdf [hereinafter Health Canada Guidance]. An articulation of the government’s pharmaceutical policy as it relates to the NOC Regulations can be found in the June 17, 2006 RIAS, which states:

The Government’s pharmaceutical patent policy seeks to balance effective patent enforcement over new and innovative drugs with the timely market entry of their lower-priced generic competitors. The current manner in which that balance is realized was established in 1993, with the enactment of Bill C-91, the Patent Act Amendment Act, 1992, S.C. 1993, c. 2.

140 C. Gaz. 24 Pt. I, 1611 (2006). *See generally* 132 C. Gaz. 11 Pt. I, 553 (1998); 133 C. Gaz. 21 Pt. II, 2355 (1999). Evidence of legislative intent regarding the “original policy intent” of encouraging development of new and innovative drugs can be found in both RIAS and related Guidance Document.

84. *Biolyse Pharma Corp. v. Bristol-Myers Squibb Co.*, [2005] 1 S.C.R. 533, ¶¶ 47, 156, 157 (Can.). Justice Binnie stated:

It has long been established that the usage of admissible extrinsic sources regarding a provision’s legislative history and its context of enactment could be examined. I held in *Francis v. Baker*, at para. 35, that “[p]roper statutory interpretation principles therefore require that all evidence of legislative intent be considered, provided that it is relevant and reliable.” Consequently, in order to confirm the purpose of the impugned regulation, the intended application of an amendment to the regulation or the meaning of the legislative language, it is useful to examine the RIAS, prepared as part of the regulatory process . . . .

*Id.* at ¶156. *See* RUTH SULLIVAN, SULLIVAN AND DRIEDGER ON THE CONSTRUCTION OF STATUTES 499•500 (4th ed. 2002).

85. *Biolyse*, [2005] 1 S.C.R. at ¶¶ 47, 156–157; *AstraZeneca Canada Inc. v. Canada (Minister of Health)*, [2006] 2 S.C.R. 560 (Can.); *ratiopharm inc. v. Wyeth and Wyeth Canada*, [2007] F.C.A. 264 (Can.).

86. 138 C. Gaz. 50 Pt. I, 3714 (2004).

87. 142 C. Gaz. 13 Pt. II, 1390 (2008).

regime came into force.<sup>88</sup>

In the United States, where pharmaceutical linkage first came into force, the purpose of Hatch-Waxman was explicitly to balance the two competing policy objectives of inducing brand pharmaceutical firms to make the investments necessary to develop new and innovative drug products while also enabling competitors to bring cheaper, generic copies of those drugs to market as soon as possible.<sup>89</sup> As noted by Senator Hatch at the time the legislation came into force said “The public receives the best of both worlds—cheaper drugs today and better drugs tomorrow.”<sup>90</sup> Therefore, in addition to stimulating pioneering drug development, a second major policy goal of linkage in the United States was to facilitate timely generic entry.<sup>91</sup> In its report on Hatch-Waxman, the Committee on the Judiciary was explicit as to what public policy grounds were involved in achieving the balance of these competing policy goals, stating that early generic availability would substantially assist in the reduction of health care costs for the poor, the under-insured, elderly, and the government as a purchaser of prescription drugs. In addition, and given the regulatory nature of the industry involved, early-working allowing a shortening of the delay of generic entry was held not to unduly encroach on the patent rights of brand firms and to properly enhance competition between brand and generic firms.<sup>92</sup>

Hence the goal of linkage in both originating jurisdictions was to facilitate timely generic entry while also stimulating the development of new and innovative drugs.

What does it mean for a drug to be “new and innovative?” When

88. In his 2003 testimony before the House of Commons Standing Committee on Industry, Science and Technology, the CEO of GlaxoSmithKline stipulated that the NOC Regulations ensured *balance* within Canada’s patent regime and encouraged *innovation* into *new* therapies. Jordan, *supra* note 3, at 66 (emphasis added). For an example of pharmaceutical literature highlighting the importance of linkage regulations see CANADA’S RESEARCH-BASED PHARMACEUTICAL COMPANIES (RX&D) INFORMATION GUIDE 2002, Section 2: Industry Issues (2002); ASTRAZENECA CAN., THE PATENT ACT & LINKAGE REGULATIONS: ESSENTIAL TOOLS FOR THE ADVANCEMENT OF MEDICAL SCIENCE IN CANADA (2009), <http://www.astrazeneca.ca/documents/en/aboutus/PatentActLinkageRegulations.pdf>.

89. Abbott Labs. v. Young, 920 F.2d 984, 991 (D.C. Cir. 1990); H.R. Rep. No. 98-857, pt. 1, at 14–15 (1984); Mylan Pharms., Inc. v. Thompson, 268 F.3d 1323, 1326 (Fed. Cir. 2001).

90. Richard Epstein & Bruce Kuhlik, *Navigating the Anticommons for Pharmaceutical Patents: Steady the Course on Hatch-Waxman*, n.24 (Univ. of Chi. L. & Econ., Working Paper No. 209, 2004) (citing Congressional Record – Senate at 23764 (August 10, 1984)).

91. Daniel R. Cahoy, *Patent Fences and Constitutional Fence Posts: Property Barriers to Pharmaceutical Importation*, 15 FORDHAM INTELL. PROP. MEDIA & ENT. L.J. 623 (2005).

92. H.R. Rep. 98-857, pt. 2, at 25 (1984).



drafting the NOC Regulations, the federal government did not provide specific definitions for these terms (in RIAS documents or otherwise), nor did it provide a Preamble as one often finds preceding legislation. The implication is that the matter was left for the courts to adjudicate or that the government did not, or would not, say one way or the other.<sup>93</sup>

According to the Oxford International Dictionary,<sup>94</sup> the word “innovate” evolved from the Latin *innovare* (1548), to make new. The term focuses on bringing forth something completely new, novel, or revolutionary into existence. The word “new,” from the Greek *véos*, Latin *novus*, and Old English *néowe*, refers to something that did not exist before; something that is brought into existence for the first time; is fresh; and not previously known. Similarly, the word “novel” (1475), from the French *nouveau* and Latin *novellum*, refers to something that is fresh, or of recent origin, of a new kind or nature that is hitherto unknown. Finally, the word “revolutionary,” from Old French and late Middle English (1450), refers to an instance of great change in a particular thing that is rare; an overthrow of the established way of doing things.

The definition for each of these words is internally consistent and contains both qualitative and quantitative aspects that may be relevant to interpretation of the NOC Regulations. The former refers to the notion that an innovative product (to use the current vernacular) is one that has not appeared before its introduction into the marketplace in any *meaningful* manner; while the latter may be taken to imply that the product is not only the *first* of its kind in existence but represents a truly *revolutionary* product rather than an incremental advance over existing products.

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93. Both the Canadian Medical Association and the Consumers Association of Canada in their evidence before the Parliamentary Committee on Bill C-91 requested that government take an evidence-based approach to research and development, and noted that no attempt was made by the government in the lead-up to Bill C-91 to empirically or objectively assess the potential impact of patent reforms on the costs and benefits to federal or provincial public health systems. *See supra* notes 5 and 55, for comments by the Minister of Consumer and Corporate Affairs that at the time Bills C-22 and C-91 were being implemented, suggest Parliament did know that it was possible to measure innovation and construct a national pharmaceutical policy with balanced incentives and rewards, deciding instead the preferable route was to eschew this approach in favor of a system with neither output metrics nor proportionality. Jordan, *supra* note 3; Harrison, *supra* note 4. *See generally Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:4 Parliament of Canada, 4:8–10, 4A:18, (Nov. 27, 1992) and *id.* at 34:5 Parliament of Canada, 5:53 (Nov. 30, 1992).

94. OXFORD INTERNATIONAL DICTIONARY OF THE ENGLISH LANGUAGE, UNABRIDGED (1958).

As noted in our Berkeley study,<sup>95</sup> while the plain meaning of the terms new and innovation are straight forward, published definitions of what should constitute an innovative drug range considerably based largely on industry affiliation. At one end, industry supporters argue that a new and innovative drug is one that merely contains a NAS,<sup>96</sup> to the slightly more stringent requirements of either being directed to First in Class therapies (irrespective of whether approval is directed to a new or follow-on drug)<sup>97</sup> or to follow-on drugs that nevertheless undergo priority review.<sup>98</sup> However, merely containing a NAS is an insufficient basis for designating a drug as pioneering or even as strongly innovative. This is because there is ample room in either definition for minor changes to previously approved medical ingredients, including salts, esters, solvates, polymorphs, and enantiomers. A similar conclusion applies to drugs that are only directed to First in Class therapies, as these can also be follow-on versions of previously marketed products containing slightly modified medical ingredients or directed to new uses within a therapeutic class. Similarly, where priority review need only be directed to drugs demonstrating moderate clinical improvement over existing therapies, it is also an insufficient proxy for strong innovation.

The most plausible definition is that a truly new and innovative drug is one approved via the new drug approval pathway, one that contains a NAS, one that undergoes some form of priority review, and one that is directed to a First in Class therapy.<sup>99</sup> Only in combination do these requirements approach a reasonable definition for a truly breakthrough or pioneering technology that would constitute a new and innovative drug, such as that contemplated by the NOC Regulations.

The second policy goal underpinning the regulations is to facilitate the timely entry of generic drugs into the marketplace. The definition of “timely” (1593), from the Old English adjective *tímlíce*, is to appear early, soon; quickly; or in good season.<sup>100</sup> Thus, when something appears in a timely manner it does so at a time that provides the greatest benefit to those for whom it appears. Given the public health goal of

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95. Bouchard 2009, *supra* note 14, at 1508.

96. J.D. Kleinke, *Commentary: Much Ado About a Good Thing*, 325 BRIT. MED. J. 1168, 1168 (2002).

97. See COHEN 2005, *supra* note 22, at 78; U.S. NAT’L RES. COUNCIL, PROSPECTUS FOR NATIONAL KNOWLEDGE ASSESSMENT, COMMITTEE ON KNOWLEDGE ASSESSMENT OFFICE OF INTERNATIONAL AFFAIRS (1996).

98. Bouchard 2009, *supra* note 14. See, e.g., PHARMACEUTICAL INNOVATION, *supra* note 21.

99. *Id.*

100. OXFORD INTERNATIONAL DICTIONARY, *supra* note 94.

facilitating generic entry for cost savings purposes (for individual consumers and institutional payers), one can reasonably assume the timeliness of generic entry refers to the earliest possible date of patent expiry pertaining to a new and innovative drug. This is consistent with the fact that the enabling section of the NOC Regulations is the infringement section pertaining to the early working provision. As noted in the June 17, 2006 RIAS:

On one end of the balance lies subsection 55.2(1) of the *Patent Act*, better known as the "early-working" exception. In the pharmaceutical industry, early-working allows second- and subsequent-entry drug manufacturers (typically generic drug companies) to use a *patented, innovative drug* for the purpose of seeking approval to market a competing version of that drug.<sup>101</sup>

As discussed in more detail below, however, the concept of early working did not,<sup>102</sup> and indeed should not,<sup>103</sup> refer to the working of *any* patent at *any* time. It was intended to refer to a specific patent on a specific drug about to come off patent protection so as to allow generic firms to prepare for timely market entry. A second element of this analysis is that a drug referred in Section 55.2(1) is not a new and innovative drug for the purposes of *all* time. It is a drug that is new and innovative at a particular time in history. The moment when this drug is no longer new or innovative, for example when it becomes the basis of SNDS submissions and follow-on drugs,<sup>104</sup> constitutes the moment in history when patents are no longer in relation to new and innovative drugs, and thus, the moment that may reasonably trigger timely generic entry.

A time-sensitive definition of patent protection for drugs that are "new and innovative" is consistent with policy debates preceding the

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101. 140 C. Gaz. Pt. I, at 1611 n.24 (2006) (emphasis added).

102. During the parliamentary debates leading up to Bill C-91, it was clear that there would only be a small number of patents, indeed most often a single or *main* patent, to contend with in the early working scenario. See generally testimony on this point by the Director General, Chemical and Bio-Industries Branch, Department of Industry, Science and Technology, *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:37 (Dec. 1, 1992) and testimony from Green Shield, *id.* at 34:7 Parliament of Canada, 7:27 (Dec. 1, 1992).

103. For the reasons why it *should not* are discussed in the review of the Supreme Court of Canada's "patent-specific" analysis, see *infra* Section IV.D.

104. For example, the conversion from a mesylate to besylate salt form, a dihydrate to monohydrate crystalline form, a tablet to capsule form, between different stereoisomers or enantiomeric forms, etc., with little or no change in bioavailability, pharmacokinetics, and therapeutic benefit.

coming into force of Hatch-Waxman in the United States. While acknowledging that multiple patents could be listed on the patent register, the Committee on Energy and Commerce, to whom the Hatch-Waxman amendment were referred by Congress, explicitly noted that the ability of brand firms to delay generic entry should be narrow both in scope and time; the proper time for generic entry being “the expiration date of the valid patent covering the original product” and that “there should be no other direct or indirect method of extending patent term.”<sup>105</sup> The Committee on the Judiciary, to whom Hatch-Waxman was also referred, acknowledged that FDA rules restricting generic entry prior to Hatch-Waxman “had serious anti-competitive effects” and that the “net result of these rules has been the practical extension of the monopoly position of the patent holder beyond the expiration of the patent.”<sup>106</sup> The Committee on the Judiciary went further regarding the multiple patent listing issue, stating that it “accepted the rationale put forward by the Committee on Energy and Commerce concerning the need to avoid multiple patent term extensions” to the effect that “the only patented product which experiences any substantial regulatory delay is the first product patent (or if there is no product patent, the first process patent).” As a result, the Committee concluded that any “subsequent patents on approved drug products are frequently not the same magnitude of innovation as occurs with respect to the initial patent” and that “on public policy and health policy grounds that only the first patent on a drug-type product should be extended.”<sup>107</sup> Thus, there is substantial evidence in both Canada and the United States that the nexus between drug approval and patents should be narrow, both in scope and time.

In choosing the words “the development of new and innovative drugs” to be one half of the balance linking patent law to food and drug law, federal governments in the United States and Canada articulated a clear public policy goal that pioneering drug development is desired in exchange for the “unusual protections” afforded to the pharmaceutical

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105. House Report No. 98-857, pt. 1 (1984). At 30, the Committee stated: article 1, section 8, clause 8 of the constitution empowers congress to grant exclusive rights to an inventor for a limited time. That limited time should be a definite time and, thereafter, immediate competition should be encouraged. For That reason, Title I of the bill permits the filing of abbreviated new drug applications before a patent expires and contemplates that the effective approval Date will be the expiration date of the valid patent covering the original Product. Other sections of title ii permit the extension of the term of a patent for a definite time provided certain conditions are met. There should be no other direct or indirect method of extending patent term.

106. H.R. 98-857, pt. 2, at 4 (1984).

107. *Id.* at 5–6.

industry by the linkage regime.<sup>108</sup> Similarly, in choosing the words “timely market entry of their lower priced generic competitors” these governments articulated a second public policy goal of cost savings,<sup>109</sup> triggered by expiry of specific patents on specific drug forms that are no longer new and innovative.

Based on the forgoing argument, it is reasonable to conclude that the “balance” sought to be effected by the NOC Regulations between food and drug law and patent law is not just a *qualitative* balance between two poles, but also a *quantitative* balance. The more reward there is on the private side of the ledger, the more there must be on the public side in order to maintain a valid legal equilibrium.

Our data indicate that generic market entry is substantially delayed by the linkage regime, and that rent-seeking behavior by brand-name pharmaceutical firms to leverage loopholes in the regime is passed on in the form of continued monopoly costs to the public. Put another way, the results of Studies 1, 2, and 3 reveal the fact that not only has the production of new and innovative drugs declined over the last decade, but also that the legal protection of drugs under the linkage regime has conversely increased compared to the protection afforded via conventional infringement grounds.

The data suggest that there are two components to the disequilibrium affected by the regulations “in operation.” First, is the increase in private rewards compared to neutral public value, and second is the delay in generic entry compared to a neutral private reward. Of note, the two components combine to produce a larger disequilibrium than either one alone.

An investigation into the qualitative and quantitative nature of the balancing of public and private benefits such as that described above is consistent with the quid pro quo of the traditional patent bargain and the fact that the enabling statute for the NOC Regulations is the Patent Act. With this in mind, the following section turns to the Supreme Court of Canada’s “patent-specific” analysis evidenced in its trilogy of cases on the NOC Regulations.

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108. The Federal Court of Canada, the Federal Court of Appeal, and the Supreme Court of Canada have repeatedly cited the language of the Supreme Court, which refers to the NOC Regulations as a “draconian regime” in its first decision on topic. *See Merck Frosst Canada Inc. v. Canada (Minister of Nat’l Health & Welfare)*, [1998] 2 S.C.R. 193, ¶ 33 (Can.).

109. As noted by the Committee on the Judiciary in its influential report (H.R. Rep. 98-857, pt. 2, at 25 (1984), the public policy grounds achieved through early generic availability included: reduction of health care costs for the poor, the under-insured, elderly, and the government as a purchaser of prescription drugs.

C. “Patent-Specific” Analysis

The qualitative and quantitative interpretation of the original policy intent advocated above supports a specific reading of the application of Section 55.2 (infringement) to a narrow range of patents per drug rather than a general reading that would lay the groundwork for a broad and potentially indefinite extension of market exclusivity for already approved pharmaceuticals. The starting point for the analysis is the enabling statute. As noted by Driedger:

It is not enough to ascertain the meaning of a regulation when read in light of its own object and the facts surrounding its making; it is also necessary to read the words conferring the power in the whole context of the authorizing statute. The intent of the statute transcends and governs the intent of the regulation.<sup>110</sup>

In its leading decisions on the linkage regime in *Biolyse* and *AstraZeneca*,<sup>111</sup> the Supreme Court of Canada narrowly constrained its analysis on drug submissions and patent listing within the terms of the Patent Act, expressly stipulating a patent-specific analysis rather than a broad inclusive analysis of drug submissions and patents supporting market exclusivity under the NOC Regulations.<sup>112</sup> The court held that while the balance sought is that between food and drug law and regulations and patent law and regulations,<sup>113</sup> the objects of patent legislation and policy take precedence when interpreting the broad ambit of the NOC Regulations. When analyzing cases under the NOC Regulations, courts are required to specifically consider the balance struck under the Patent Act whereby the public gives an inventor the right to monopoly protection of their invention in exchange for

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110. ELMER A. DRIEDGER, CONSTRUCTION OF STATUTES 247 (2d ed. 1983). For discussion of Driedger’s approach to statutory interpretation in the context of NOC Regulations analysis, see *Biolyse Pharma Corp. v. Bristol-Myers Squibb Co.*, [2005] 1 S.C.R. 533 (Can.); *AstraZeneca Canada Inc. v. Canada (Minister of Health)*, [2006] 2 S.C.R. 550, ¶ 26 (Can.).

111. *Biolyse*, [2005] 1 S.C.R. at ¶ 26; *AstraZeneca*, [2006] 2 S.C.R. at ¶ 36.

112. *AstraZeneca*, [2006] 2 S.C.R. at ¶ 39. A “patent-specific analysis” was recently confirmed by Health Canada in its 2009 Guidance Document relating to the NOC Regulations. HEALTH CANADA GUIDANCE, *supra* note 83, at 26. In addition to acknowledging that a “patent-specific analysis” is necessary when interpreting the NOC Regulations, the government further stated that only certain patents are “eligible” for protection under the NOC Regulations, indicating that not all patents fall within the purview of the regulations. *Id.* at 28. See also *AstraZeneca*, [2006] 2 S.C.R. at ¶ 39; *Ferring Inc. v. Canada (Minister of Health)*, [2008] 1 F.C.R. 19, ¶¶ 51–57 (Can.).

113. *AstraZeneca*, [2006] 2 S.C.R. at ¶ 39.

disclosure of socially valuable information.<sup>114</sup> In *Biolyse*, the court held that when contemplating inventions in the field of patented medicines, we must be mindful of the fact that Parliament was concerned not only with the balance between inventors and potential users, but also “that between protection of intellectual property on the one hand and, on the other hand, the desire to reduce health care costs while being fair to those whose ingenuity brought the drugs into existence in the first place.”<sup>115</sup> As a result, claims such as those by Industry Canada, that poor or otherwise inefficient working of the NOC Regulations resulting in evergreening of older products can be counter-balanced by the benefits of a patent regime that gives multi-national firms confidence in Canada,<sup>116</sup> must be tempered by legal assessment of relevant evidence pertaining to the functioning of the regulations in light of legislative intent. This latter statement is consistent with amendments to the NOC Regulations specifically intended to limit evergreening through abuse of the automatic stay provision.<sup>117</sup>

If the public benefits of innovation are raised under the linkage regulations through the terms of the patent bargain,<sup>118</sup> then how much does one ask for in exchange for the unusual protections of the linkage regime? The term “patent bargain” is usually used to refer to a grant of a limited patent monopoly in exchange for public disclosure of socially valuable knowledge.<sup>119</sup> In a public health context, where drug approval and drug patenting are linked, the essence of the patent bargain may be viewed as the exchange of extended patent protection for a socially beneficial level of pharmaceutical innovation that is proportional to the benefit to firms of extending market exclusivity. Thus, the public expects, and should expect, something of substantial value in exchange for extended patent protection and monopoly pricing. In other words, there should be a strong functional legal nexus between public health

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114. *Biolyse*, [2005] 1 S.C.R. at 533.

115. *Biolyse*, [2005] 1 S.C.R. at 533, ¶ 2.

116. 142 C. Gaz. 13 Pt. II, 1390, 1593 (2008). This is a similar statement to that found in all post-2004 RIAS documents that the NOC Regulations provide “stability, predictability and competitiveness” to Canada’s pharmaceutical patent regime. *See generally* 138 C. Gaz. 50 Pt. I, 3714 (2004); 140 C. Gaz. 24 Pt. I, 1601 (2006); 142 C. Gaz. 13 Pt. I, 1390, 1588 (2008).

117. *See* 132 C. Gaz. 11 Pt. I, 553 (1998); 133 C. Gaz. 21 Pt. II, 2355 (1999); 138 C. Gaz. 50 Pt. I, 3714 (2004); 140 C. Gaz. 24 Pt. I, 1601 (2006); 142 C. Gaz. 13 Pt. II, 1390, 1588 (2008).

118. Bouchard 2010, *supra* note 13.

119. *Graham v. John Deere Co.*, 383 U.S. 1, 8 (1966); *KSR Int’l v. Teleflex, Inc.*, 550 U.S. 398 (2007); *Whirlpool Corp. v. Camco, Inc.*, [2000] 2 S.C.R. 1067 (Can.). For general discussion, see Ron A. Bouchard, *KSR v. Teleflex Part I: Impact of U.S [sic] Supreme Court Patent Law on Canadian Intellectual Property and Regulatory Rights Landscape*, 15 HEALTH L.J. 221 (2007) [hereinafter Bouchard KSR Part 1].

policy and patent policy.

The social benefits of approval-patenting linkage are also implied by the obligation on courts to carefully scrutinize pharmaceutical patents to determine if they properly merit the grant of a monopoly privilege in light of the substantial public interest at stake,<sup>120</sup> as well as the observation that the linkage regulations are deemed to involve “special enforcement provisions” that operate well beyond the purview of traditional patent law.<sup>121</sup> As stated in *Whirlpool*,<sup>122</sup> the bargain between patentee and public is in the interest of both sides only where the patentee receives a monopoly reward that is proportional to what it discloses to the public; a patentee who evergreens an invention via successive patents on uninventive additions prolongs its monopoly beyond what the public has agreed to pay.

Two cases in particular are instructive about how narrow the functional linkage between the rights of the inventor and those of the public in the context of the patent bargain should be. In *AstraZeneca v. Canada*, the Supreme Court held that the listing provisions of the NOC Regulations are linked only to a “specific” drug submission rather than a general submission. The court held that a general listing provision would allow undue evergreening,<sup>123</sup> which would be inconsistent with the intent of Parliament in enacting the NOC Regulations. A broad interpretation of the listing provision was seen by the court to undermine the balance sought by Parliament between the objectives of food and drug law and patent law,<sup>124</sup> with the result that the public would not derive appropriate benefit from patent legislation—in this case from properly listed patents. The court stipulated that this scenario “offends the ‘balance’ inherent to the quid pro quo” in that the “patentee takes too much in exchange for a weakly innovative invention.”<sup>125</sup>

In other words, the functional legal nexus between patent law and food and drug law was insufficiently narrow to support the extension of a patent monopoly on weakly innovative drugs via the linkage regime.

The court also held that ambiguity as to the specific intent of a

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120. *Farbwerke Hoechst Aktiengesellschaft Vormals Meister Lucius & Bruning v. Comm’r of Patents* [1966] S.C.R. 604 (Can.).

121. 140 C. Gaz. 24 Pt. I, 1598 (2006).

122. *Whirlpool*, [2000] 2 S.C.R. at ¶ 37 (Can.). See also *Free World Trust v. Électro Santé Inc.*, [2000] 2 S.C.R. 1024, ¶ 13 (Can.).

123. *AstraZeneca Canada Inc. v. Canada (Minister of Health)*, [2006] 2 S.C.R. 550, ¶ 23 (Can.).

124. *Id.* at ¶ 39.

125. *Id.* at ¶ 39.



regulation does not have to manifest itself in specific statutory text in order to be properly considered by the court. Rather, such ambiguity should be analyzed within the entire context of the legislation.<sup>126</sup> Importantly, the court overruled a general listing requirement notwithstanding the acceptable industrial strategy of firms to evergreen products by “adding bells and whistles to a pioneering product even after the original patent for [the] pioneering product has expired.”<sup>127</sup> This result was based on the finding that an overly broad interpretation of the NOC Regulations was inconsistent with the narrow terms of Parliament’s intent in enacting the regulations and offended the quid pro quo of the traditional patent bargain.

A similar result was obtained in *Biolyse v. Bristol-Myers Squibb* (BMS) again using a patent-specific analysis. Here the Supreme Court dealt with what constituted a brand-name versus a generic “submission” and, thus, whether a second-entry firm needs to litigate all listed patents prior to market entry. BMS argued that a drug submission should be construed broadly to include all submissions, whereas Biolyse argued that the term should be interpreted narrowly. While the word “submission” was seen to provide an entry into analysis of statutory language governing submissions, the court noted that the term submission was not specifically defined in the regulations. Under the terms of its earlier decision in *Bell ExpressVu*,<sup>128</sup> the court saw its duty to consider the entire context of the provision and enabling legislation before undertaking a specific analysis of the term.

Taking a purposive approach, the court held that the term submission should be analyzed in its narrow sense rather than a broad general sense. A general interpretation was seen to lead to the absurd result whereby a submission by one firm relevant to a medication encompassed all further submissions relating to that medication, thus allowing the original patentee to evergreen its product via ever diminishing minor improvements. This scenario was seen to push the regulations well beyond its stated purpose, stifle competition and innovation in the pharmaceutical industry, and yield a result at odds with legislative intent.<sup>129</sup> The section was held to be *ultra vires* based on breach of the quid pro quo such that the patentee could extend its monopoly far beyond what its skill and ingenuity contributed to the

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126. *Id.* at ¶¶ 29–30.

127. *Id.* at ¶ 39.

128. *Bell ExpressVu Ltd. v. Rex*, [2002] S.C.R. 42, ¶ 10 (Can.).

129. *Biolyse Pharma Corp. v. Bristol-Myers Squibb Co.*, [2005] 1 S.C.R. 533, ¶¶ 65–67 (Can.).

public. As with *AstraZeneca*, the court's decision was patent-specific and hinged on a narrow rather than general nexus between drug approval and drug patenting.

A strong lesson from *Biolyse* and *AstraZeneca* is that critical to analysis of whether pharmaceutical linkage is a success or failure in achieving its twin policy goals is the long-held exercise in patent jurisprudence to ensure the patent owner is not getting more of a monopoly than the public bargained for despite claims of the patentee (and its industry and government supporters) to the contrary.<sup>130</sup> Innumerable cases have been brought before the courts based more on imagined, or hypothetical, inventions rather than real ones. When only patent law is construed, the difference is whether or not the inventions satisfy the requirements set out in relevant patent legislation. This is not so with regard to the NOC Regulations, which provide for a *specific* legal and functional link among the drug approved, its relevant patents, and whether they are listed on the patent register. The unique nature of the interrelationship between the Food and Drug Act, Food and Drugs Regulations, Patent Act, and Patented Medicines (Notice of Compliance) Regulations was recognized in this regard by the federal government in its lengthy 2004 RIAS: "Despite their seemingly competing policy objectives, it is important that neither instrument [Patent Act, NOC Regulations] be considered in isolation, as the intended policy can only be achieved when the two operate in a balanced fashion."<sup>131</sup>

Based on the foregoing jurisprudence, it is plausible to argue that the interpretation of what constitutes sufficient grounds for the "special protection" afforded by the NOC Regulations may be seen to differ from the threshold for patentability per se.

Indeed, the difference between real and imagined inventiveness has been previously recognized by regulators in the context of the NOC Regulations and used to negate the protection of the regulations for inventions where a patentee failed to demonstrate a strong connection between the invention sought to be protected and the product sought to be approved.<sup>132</sup> This suggests that the concept of early working should

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130. *Free World Trust v. Électro Santé Inc.*, [2000] 2 S.C.R. 1024, ¶ 42 (Can.).

131. 138 C. Gaz. 50 Pt. 1, 3712 (2004).

132. 140 C. Gaz. 24 Pt. 1, 1598, 1611–12 (2006). The government specifically stipulated that:

[A] temporal connection between the invention sought to be protected and the product sought to be approved. This ensures that patents for inventions discovered after the existence of a product do not pre-empt generic competition on that product. Similarly, the relevance requirement limits the protection of the

not refer to the working of *any* patent at *any* time. Rather, the early working provision specifically, and hence the empirical outputs of the linkage regime more generally, should only encompass patents relating to a *specific* drug that is new and innovative for the first time in history. The early working provision should not encompass patents that form the basis of SNDS submissions and follow-on drugs. Ironically, this approach was supported by the federal government in its testimony before the Parliamentary Committee on Bill C-91. That testimony stated that a new and innovative drug was said to have “[one] main patent” and “w[h]en that main patent expires, anyone may copy that product and bring it to market.”<sup>133</sup> As discussed above, a similar conclusion was reached by both the Committee on Energy and Commerce and the Committee on the Judiciary at the time the originating Hatch-Waxman regime came into force.

In light of government reports and jurisprudence on topic, one can reasonably conclude that the linkage regime was never intended to act as a vehicle for continuous evergreening of blockbuster products. At least with regards to Canadian law, pharmaceutical linkage was intended to provide for international harmonization of Canada’s patent laws balanced by a narrow (patent-specific) exemption to the infringement section of the Patent Act in order to allow the early working of generic drugs prior to expiration of the main patent on a given drug. To paraphrase Justice Binnie in *Free World Trust*,<sup>134</sup> there is

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PM(NOC) Regulations to that which the innovator has invested time and money to test and have approved for sale. This prevents hypothetical innovation from impeding generic market entry and encourages innovators to bring their latest inventions to market. Finally, in only allowing patents to be listed which contain claims for the medicine or its use, the subject matter requirement makes it clear that innovations without direct therapeutic application, such as processes or intermediates, do not merit the special enforcement protection of the PM (NOC) Regulations.

*Id.* at 1612–13.

133. *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:8 Parliament of Canada, 8:37 (Dec. 1, 1992).

134. *Free World Trust v. Électro Santé Inc.*, [2000] 2 S.C.R. 1024, ¶ 42 (Can.). The court states:

The patent system is designed to advance research and development and to encourage broader economic activity. Achievement of these objectives is undermined however if competitors fear to tread in the vicinity of the patent because its scope lacks a reasonable measure of precision and certainty. A patent of uncertain scope becomes “a public nuisance” . . . .

*R.C.A. Photophone, Ltd. v. Gaumont-British Picture Corp.* (1936), 53 R.P.C. 167, 195 (Eng. C.A.).

Potential competitors are deterred from working in areas that are not in fact covered by the patent even though costly and protracted litigation (which in the case

a high economic cost attached to taking an overly broad approach to assessing the nexus between drug approval and drug patenting. Continuing the analogy, we might also say that it is the proper policy of patent law to keep the legal nexus between the scope of patent protection and the scope of innovation narrowly construed rather than broadly construed, and to assess the integrity of this nexus in light of all relevant empirical evidence. Otherwise, as at issue in *Biolyse* and *AstraZeneca*, the pharmaceutical linkage regime may stifle innovation, operate beyond its stated purpose, and yield a result that is at odds with legislative intent.

#### D. Statutory Interpretation

The purpose of this Section of the Article is to raise the possibility that empirical evidence demonstrating that legislation does not achieve its ends can support the conclusion that the legislation is invalid or in need of substantial amendment in order for it to remain *intra vires*. An ancillary goal is to explore whether there are aspects of statutory interpretation that illuminate an investigation into whether the NOC Regulations are meeting the stated goals of stimulating the development of new and innovative drugs and facilitating timely entry of generic drugs, and the manner in which this question may be assessed from a purposive perspective.

According to the principles of purposive analysis as recently reviewed by Hutchinson in the context of intellectual property,<sup>135</sup> the essence of ordinary language is paramount to the exercise of statutory interpretation. The ordinary language of a statute or regulation is informed contextually by the scheme and purpose as well as evidence of statutory intent.<sup>136</sup> Referred to as “external context,”<sup>137</sup> the interface between original policy intent and the consequences thereof in the real world informed by the original policy intent refers to “how the

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of patent disputes can be very costly and protracted indeed) might confirm that what the competitors propose to do is entirely lawful. Potential investment is lost or otherwise directed. Competition is “chilled”. The patent owner is getting more of a monopoly than the public bargained for. There is a high economic cost attached to uncertainty and it is the proper policy of patent law to keep it to a minimum.

*Id.*

135. See generally Cameron Hutchinson, *Which Kraft of Statutory Interpretation? A Supreme Court of Canada Trilogy on Intellectual Property Law*, 46 ALBERTA L. REV. 1 (2008).

136. *Id.* at 7.

137. RUTH SULLIVAN, SULLIVAN AND DRIEDGER ON THE CONSTRUCTION OF STATUTES 20 (4th ed. 2002).

legislation works operationally.”<sup>138</sup> As a reminder, the twin policy goals underpinning the NOC Regulations are to stimulate the development of new and innovative drugs and to facilitate timely generic entry. In the present circumstances, the term *external context* could thus reasonably be assumed to encompass empirical evidence of the extent and manner in which the NOC Regulations affect (1) the production of new and innovative remedies and (2) the timely entry of generic remedies once the original product patent has expired. Considerations of external context are those which privilege the setting in which a law *operates*, i.e., empirically, as a response to a set of evolving institutions and relationships.<sup>139</sup>

The construction of law as a dynamic and adaptive (or maladaptive) system with multiple interconnected and interdependent nodes is consistent with arguments made on the potential impact of Bill C-91 by the Canadian Association of Consumers (CAC) discussed in Section II.A. *supra*. Of particular relevance, the CAC pointed out that in exchange for patent reforms including linkage Canada could possibly be contributing to capital market protectionism by multinational pharmaceutical firms, a likely preference by firms and regulators for low-level innovations (Me Too and other follow-on drugs), as well as minimal positive social welfare outcomes given the preference for enhanced follow-on innovations. These concerns were echoed in the testimony of U.S.-based economist Stephen Schondelmeyer who underscored the potential of pharmaceutical linkage to result in significantly enhanced market exclusivity periods and cautioned the Parliamentary Committee to think through the issue of unintended consequences when constructing a system of innovation where new drug development and generic entry are fundamentally tied to patents on older products.

The notion of law as a complex system can also be seen in selected writings of Fuller and Dworkin to the extent that the purpose, indeed the validity, of law may be ascertained by the evolving context in which it operates.<sup>140</sup> The notion that law is “alive” rather than stagnant draws strong parallels to legal and other social sciences scholarship

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138. Hutchinson, *supra* note 135, at 7.

139. *Id.* at 7–8.

140. *Id.* at 27 (citing WILLIAM N. ESKRIDGE, PHILIP P. FRICKEY & ELIZABETH GARRETT, *LEGISLATION AND STATUTORY INTERPRETATION* 221–30 (2d ed. 2006)) (suggesting that statutes may evolve in ways contrary or against the initial intent, allowing for an adaptive assessment of the validity of a law against contemporary evidence of its operation or functioning).

demonstrating law to be a dynamic complex adaptive system.<sup>141</sup> In such systems, law-in-operation is strongly contingent on positive and negative feedback loops that impact system performance,<sup>142</sup> including systems of intellectual property law and biomedical innovation.<sup>143</sup>

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141. JOHN H. MILLER & SCOTT E. PAGE, *COMPLEX ADAPTIVE SYSTEMS: AN INTRODUCTION TO COMPUTATIONAL MODELS OF SOCIAL LIFE* 9 (2007).

In a complicated world, the various elements that make up the system maintain a degree of independence from one another. Thus, removing one such element [which reduces the level of complication] does not fundamentally alter the system's behavior apart from that which directly resulted from the piece that was removed. Complexity arises when the dependencies among the elements become important. In such a system, removing one such element destroys system behavior to an extent that goes well beyond what is embodied by the particular element that is removed. Complexity is a deep property of a system, whereas complication is not.

*Id.* at 9.

142. Feedback interactions in complex systems have received increased attention in recent years. *See generally* ALBERT-LASZLO BARABÁSI, *LINKED: HOW EVERYTHING IS CONNECTED TO EVERYTHING ELSE AND WHAT IT MEANS FOR BUSINESS, SCIENCE, AND EVERYTHING ELSE* (2003) (investigating the role of feedback in biological and social networks, including corporations and living organisms, producing system fitness); JAMES GLEICK, *CHAOS: MAKING A NEW SCIENCE* (1987) (describing order and chaos generally and how complex systems balance the two through adaptation and positive and negative feedback loops); JOHN H. HOLLAND, *ADAPTATION IN NATURAL AND ARTIFICIAL SYSTEMS* (MIT Press 1992) (1975) [hereinafter HOLLAND 1992] (outlining the importance of adaptive mechanisms in natural and artificial systems to the growth and destruction of complex systems); JOHN H. HOLLAND, *HIDDEN ORDER: HOW ADAPTATION BUILDS COMPLEXITY* (1995) [hereinafter HOLLAND 1995] (discussing adaptation in complex adaptive systems and how order and disorder are often balanced at subtle levels in these systems); STEVEN JOHNSON, *EMERGENCE: THE CONNECTED LIVES OF ANTS, BRAINS, CITIES, AND SOFTWARE* (2001) (discussing the characteristics of emergent systems, including the role of positive and negative feedback loops in governing de-centralized system growth and adaptation); STUART KAUFFMAN, *AT HOME IN THE UNIVERSE: THE SEARCH FOR THE LAWS OF SELF-ORGANIZATION AND COMPLEXITY* (1995) (investigating the conditions that give rise to the growth and destruction of complex adaptive systems and describing how optimal complex adaptive systems are balanced on the edge of chaos); GRÉGOIRE NICOLIS & ILYA PRIGOGINE, *EXPLORING COMPLEXITY: AN INTRODUCTION* (1989) (addressing the problem of complexity in using mathematical modeling and the role of essentially irreducible uncertainty in complex systems); M. MITCHELL WALDROP, *COMPLEXITY: THE EMERGING SCIENCE AT THE EDGE OF ORDER AND CHAOS* (1992) (discussing the role of the interrelation and inter-dependence of players, including individuals and institutions, in complex adaptive systems and showing that systems of this nature are never in stasis, but rather always continually evolving); Brian W. Arthur, *Positive Feedbacks in the Economy*, 262 SCI. AM. 92, 92–99 (1990) (discussing the presence of feedback in producing order and simplicity even in the most complex economic systems).

143. Bouchard 2009, *supra* note 14; Ron A. Bouchard, *KSR v. Teleflex Part 2: Impact of U.S [sic] Supreme Court Patent Law on Canadian and Global Systems-Based Innovation Ecologies*, 15 HEALTH L.J. 247, 274 (2007); Ron A. Bouchard, *Living Separate and Apart is Never Easy: Inventive Capacity of the PHOSITA as the Tie that Binds Obviousness and Inventiveness in Pharmaceutical Litigation*, 4 OTTAWA L. & TECH. J. 1 (2007) [hereinafter Bouchard 2007b]; Ron A. Bouchard, *Reflections on the Value of Systems Models for Regulation of Medical Research and Product Development*, 17 HEALTH L. REV. 30, 32 (2008).

Another principle of statutory interpretation that may be particularly relevant to analysis of the linkage regime is that interpretation of legislative intent entails an understanding of what “mischief” the statute or regulation was intended to remedy at the time it was enacted.<sup>144</sup> Review of the matters before the House of Commons Legislative Committee on Bill C-91 indicate a clear concern with stimulating the production of globally competitive innovative pharmaceutical technologies balanced by the cost considerations of promoting early generic entry. These goals are entirely consistent with the original policy intent underpinning the regulations enumerated in RIAS documents, ranging from 1993 to the present, to balance the production of new and innovative drugs with timely entry of generic products. Important to the type of balancing function inherent in the NOC Regulations, Parliament is assumed to avoid promulgating laws and regulations that conflict with one another.<sup>145</sup> Implicit in both the purposive and mischief analyses is the recognition of *indeterminate* considerations when making law and public policy that cannot be predicted,<sup>146</sup> yet which nevertheless must be accounted for in later assessments of legislative purpose or effect.

When courts are presented with competing interpretations (i.e., general or specific; Patent Act or Food & Drugs Act; health policy v. industrial policy), the clear choice is one that accords most substantively with the legislative purpose and one that is consistent with an interpretation of a given statute or regulation as a “workable whole.”<sup>147</sup> In other words, the law and policy of the legislation or regulation need to operate consistently with one another from an operational perspective. As noted by Fuller:

The troublesome cases are in reality resolved not in advance by the legislator, but at the point of application. This means that in applying the statute the judge or police sergeant must be guided not simply by the words but also by some conception of what is fit and proper to come into the park; conceptions of this sort are implicit in the practices and attitudes of the society of which he is

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144. Hutchinson, *supra* note 135, at 7–8 (citing RANDAL N. GRAHAM, STATUTORY INTERPRETATION: THEORY AND PRACTICE 31 (2001)).

145. Hutchinson, *supra* note 135, at 7.

146. *Id.* at 21.

147. LON L. FULLER, ANATOMY OF THE LAW (1968) [hereinafter ANATOMY]; Lon L. Fuller, *Positivism and Fidelity to Law – A Reply to Professor Hart*, 71 HARV. L. REV. 630, 667 [hereinafter *Fidelity*]. For a discussion of Fuller’s work in the context of intellectual property litigation, see Hutchinson, *supra* note 135, at 22–24.

a member. . . . All this adds up to the conclusion that *an important part of the statute in question is not made by the legislator, but grows and develops as an implication of complex practices and attitudes which may themselves be in a state of development or change.*<sup>148</sup>

As implied in the passage from Fuller, the purpose and intent of a statute or regulation is not static. Rather, it represents a dynamic process of refining and clarifying means and ends through a system of positive and negative feedback loops.<sup>149</sup> In other words, the intent and meaning of legislation or regulation is how it operates “in the lives of people affected by it,” not theoretically or hypothetically as an isolated idea or even goal. This, importantly, includes objective evidence of the operation of statutes and regulations such as empirical evidence of contextual operational efficiency.<sup>150</sup>

A final point, which has not escaped the notice of the Supreme Court of Canada<sup>151</sup> or the U.S. Federal Circuit,<sup>152</sup> is that courts are not the only legal authorities deciding whether legislation or regulations are valid or invalid. When faced with growing evidence of the lack of success of any legal vehicle, it is the role of the legislature to learn and dynamically adapt to external signals relating to its original policy intent, and to decide *rationally* in an *evidence-based manner* whether to abandon either the law or the original policy intent given objective evidence of how a statute or regulation operates in the ‘real world.’ Where objective empirical evidence such as that reviewed from Studies 1, 2, and 3 shows that the vehicle is operating in contrast to its stated and dynamically interpreted goals, it may be *ultra vires*<sup>153</sup> or otherwise operating outside of its stated ambit.<sup>154</sup>

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148. See ANATOMY, *supra* note 147, at 59 (emphasis added). As noted by Hutchinson, “[t]he process of interpreting a statute is not just drawing out what legislators put into it but adjusting the statute to the implicit demands and values of the society to which it is to be applied.” See Hutchinson, *supra* note 135, at 24 n.129. “In this sense it may be said that no enacted law ever comes from its legislator wholly and fully ‘made.’” *Id.*

149. Hutchinson, *supra* note 135, at 23 (referring to *Fidelity*, *supra* note 147, at 668.)

150. Hutchinson, *supra* note 135.

151. Virtually every domestic legal commentator and lawyer writing or litigating this issue has referenced the *Merck* court’s description of the NOC Regulations as “draconian.” See *Merck Frosst Canada Inc. v. Canada* [1998] 2 S.C.R. 193, ¶ 33 (Can.).

152. *Roche Prods. Inc. v. Bolar Pharmaceutical Co.*, 733 F.2d 858 (E.D.N.Y. 1984).

153. *Biolyse Pharma Corp. v. Bristol-Myers Squibb Co.*, [2005] 1 S.C.R. 533 (Can.).

154. *AstraZeneca Canada Inc. v. Canada* (Minister of Health), [2006] 2 S.C.R. 550 (Can.).



*E. Revisiting the Empirical Data*

In the discussion above, we saw that courts look favorably on evidence relating to how a statute or regulation operates in the real world, and that law can be viewed in the context of statutory interpretation as a dynamic legal construct that may or may not evolve away from its stated goal or purpose. What, then, is the evidence that operation of linkage regulations is inconsistent with the intent of the federal government to encourage the development, or even to simply protect patents relating to, new and innovative drugs? Indeed, there are two major sets of observations from our empirical work to suggest that the operation of the linkage regulations is inconsistent with the goal underpinning the linkage regime. The first set of observations relates to drug patenting and the specific levels of innovation supported by these patents. The second set of observations relates to how, in combination, drug approval, drug patenting, and the pharmaceutical linkage regime act in a coordinated manner to increase the effective period of market exclusivity to the detriment of timely generic entry.

First, we observed a time-dependent decrease in new drug development over a nearly ten-year period, well after the NOC Regulations came into force. This was accompanied by a concomitant increase, in some cases non-linear, in the development of follow-on drugs. The data reviewed above indicate that these trends have occurred seemingly independently of strong time-dependent trends in drug patenting, patent listing, and in drug approvals, consistent with the principles of emerging lifecycle regulatory models of drug regulation. The results demonstrate that pharmaceutical firms, when they so desire, are capable of responding rapidly and strongly to regulatory incentives in the context of drug regulation, but that this responsiveness has not extended to increasing the production of new and innovative drugs. An additional observation is that when drug approval data are analyzed cumulatively, there is a vanishingly small fraction (1.87%) of brand-name drugs that are truly “new and innovative.” It is difficult to believe that when Parliament stipulated that only patents on new and innovative drugs were to be protected via the new pharmaceutical linkage law it had this low level of innovation in mind. Here, it is important to bear in mind that, unlike other industries, incremental innovations that have little or no therapeutic value to individual patients may nevertheless be used as tools to extend the market exclusivity for blockbuster drugs with broad social value that would otherwise come off patent.

The second primary finding of our work is that operation of the

NOC Regulations increases the effective period of patent protection by at least two-fold beyond the normal period. As such, the evidence suggests that the linkage regulations are being used as more of a sword than a shield by pharmaceutical firms. The degree of protection offered is indiscriminate, and is not specific to high value inventions. Indeed, the observation in both the U.S. and Canada that up to 75% of listed patents are invalid when litigated on the merits<sup>155</sup> supports the conclusion that the functional nexus between drug approval and drug patenting need only be very weak (i.e., general) to support a significant extension of the patent monopoly for drugs coming off patent protection under the NOC Regulations. This scenario is worsened by a weak relevance standard for patent listing,<sup>156</sup> particularly one that permits listing of multiple patents on follow-on drugs with little change in benefit:risk. Thus, not only has the linkage regime not resulted in the development of new and innovative drugs, it has also failed to stimulate the “timely market entry of generic drugs.” Therefore, both limbs of the balance inherent in the original policy intent underpinning the linkage regime are offended.

Supporting the conclusion above is the finding that patenting of drugs by pharmaceutical firms has escalated substantially since the coming into force of the NOC Regulations, providing increasing fodder for the patent listing and automatic stay mechanisms under the regulations. Related to this is the finding that cumulative patenting and patent listing have converged strongly over time, and that the delay between drug approval and patent listing has declined to the point that the patent listing now seems a better proxy of drug development in Canada than patenting per se. Trends in new and follow-on drugs were not altered by the increasing application of the principles of lifecycle regulation, which, like the NOC Regulations, is also strongly premised on the production of new and innovative drug products in exchange for strong intellectual property and regulatory rights.<sup>157</sup> Thus, in the

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155. EDWARD HORE, PATENTLY ABSURD: EVERGREENING OF PHARMACEUTICAL PATENT PROTECTION UNDER THE PATENTED MEDICINES (NOTICE OF COMPLIANCE) REGULATIONS OF CANADA'S PATENT ACT (2004), [http://www.canadiangenerics.ca/en/news/docs/patently\\_absurd\\_04.pdf](http://www.canadiangenerics.ca/en/news/docs/patently_absurd_04.pdf); Andrew A. Caffrey, III & Jonathan M. Rotter, *Consumer Protection, Patents and Procedure: Generic Drug Market Entry and the Need to Reform the Hatch-Waxman Act*, 9 VA. J.L. & TECH. 1, 13, ¶ 27 (2004); Edward Hore, *A Comparison of U.S. and Canadian Laws as They Affect Generic Pharmaceutical Entry*, 55 FOOD & DRUG L.J. 373 (1999–2000).

156. 142 C. Gaz. 13 Pt. II, 1390 (2008) (clarifying judicial rulings on topic in 2006 by the Supreme Court of Canada in *AstraZeneca* and the Federal Court of Appeal in *Wyeth Canada v. ratiopharm, inc.*, [2008] 1 F.C.R. 447 (Can.)).

157. Ron A. Bouchard & Monika Sawicka, *The Mud and the Blood and the Beer*:

absence of a reward system that is proportional to the degree of innovation, lifecycle-based drug regulation is not likely to alter the profile of domestic drug development.

Findings from empirical studies such as those in Studies 1, 2, and 3 support the conclusion that the patterns for new and follow-on drugs may not be reflective, as claimed by industry and its supporters, of low hanging fruit already being picked, or escalating costs of drug development. This does not mean that a significant fraction of the low-hanging fruit has not been picked or that drug development has not become more expensive over time. Rather, results demonstrating a time-gated and increasing focus by firms on follow-on drug development, and on broadening the scope and number of patents, patent type classifications, and therapeutic classifications supporting them, suggest that firms may be aiming *ex ante* at discrete legal targets provided for by law. In the absence of demonstrable intent by government otherwise, this would be of no concern. However, in both the United States and Canada, federal governments have in fact stated that the twin goals of pharmaceutical linkage are to provide strong patent protection for new and innovative drugs while also facilitating rapid generic entry, and that these goals are to be achieved in the form of a specific legal nexus between drug approval and drug patenting informed by legal and policy grounds underpinning the legislation.

Contrary to the original policy behind the NOC Regulations, brand-name firms appear to have decreased their innovative output following the coming into force of the linkage regime while at the same time engaging in increased evergreening of already appropriated technologies using the linkage regulations as the preferred vehicle for patent extension. The empirical data show that, at best, the linkage between patent law and food and drug law is general rather than specific in nature. This is indicative of a weak legal and functional nexus between the scope of innovation and scope of patent protection; thus, raising the possibility that the NOC Regulations might, in principle, infringe the quid pro quo of the patent bargain and produce a result that is at odds with legislative intent.

Based on the data presented thus far, one can argue that both ends of the balancing function of the linkage regime (stimulating new and innovative drug development and facilitating timely entry of generic drugs) are operating poorly or at least very inefficiently. On the one hand, generic competition is being stifled owing to a two-fold increase in

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*Canada's Progressive Licensing Framework for Drug Approval*, 3 MCGILL J.L. & HEALTH 49, 51 (2009).

the term of patent protection under the regulations on patents that are weakly relevant to the reference product and that are often invalid when litigated on the merits. On the other, strong intellectual property protection is consistently and increasingly being afforded under the regulations for patents that are not in relation to new and innovative drugs, including those with a paradoxical approval-patent linkage. As suggested earlier, this suggests that there are two components to the disequilibrium affected by the regulations “in operation.” First, is the increase in private rewards compared to neutral public value, and second is the delay in generic entry compared to a neutral private reward. The two components combine to produce a larger disequilibrium than either one alone.

An observation that remains politically charged to this day, for jurisdictions with pharmaceutical linkage or those contemplating bringing into force some form of linkage, is that drug development by domestic firms over the last decade has been strongly focused on technology appropriation. This is somewhat ironic, as one of the major concerns of policy-makers in the early stages of development of the NOC Regulations was to “thwart” appropriation by generic drug companies of innovative technologies propagated by brand-name drug companies,<sup>158</sup> typically articulated as “rights piracy.” As discussed above, the term “appropriation” is usually used to refer to a party’s ability to capture profits generated from their own inventions or related inventions.

The data in Studies 1, 2, and 3 indicate that not only are generic firms not unduly appropriating innovative technologies, but even if obtaining an NOC based on bioequivalence grounds could be construed as appropriation, generic firms are only following the lead of brand-name firms who are themselves focusing on follow-on approvals while at the same time decreasing new drug development activities. This led us to conclude in our McGill study<sup>159</sup> that the domestic limbs of multinational pharmaceutical companies are “doing more with less.” As such, not just brand-name firms, but all forms of domestic pharmaceutical companies we studied over the course of nearly a decade are focusing a progressively greater share of their patenting and regulatory approval energy on appropriating, or extending the value, of existing technologies over time, presumably relying on the acquisition of

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158. *Biolyse Pharma Corp. v. Bristol-Myers Squibb Co.*, [2005] 1 S.C.R. 533, ¶ 45 (Can.) (citing *Apotex Inc. v. Canada*, [1994] 1 F.C. 742 (Can.), *aff’d* [1994] 3 S.C.R. 1100 (Can.)).

159. See generally Sawicka & Bouchard, *supra* note 11.

pioneering biotechnology firms as their technologies crystallize through clinical trials.

Finally, the results reviewed in this Article have some important implications for innovation theory in general, which holds that follow-on or incremental innovation is equally important to overall domestic productivity and prosperity as pioneering innovation. However, unlike other industries, follow-on innovations in the pharmaceutical sector often have little or no therapeutic benefit for the population at large compared to existing drug products. While this is obviously not true for all follow-on drugs, when the system is effectively gamed, the multiple patent listing provision in combination with weak evidentiary requirements for new and follow-on drug approval can be used to powerfully extend market exclusivity for blockbuster drugs in a manner that impacts drug pricing for both public and private payers. Patents on products within a cluster can be used for this purpose either by providing the basis for follow-on drug submissions or by providing a large pool for patenting listing purposes. In either case, breakthrough innovation is diminished at the same time as the timely entry of generic products is delayed. Thus, as noted *supra*, the social consequences of a regulatory preference for follow-on drugs may be much greater in the public health sector than other sectors of the economy.

### III. IMPLICATIONS FOR PHARMACEUTICAL LAW AND POLICY

#### *A. Theory of Linkage-Based Drug Development*

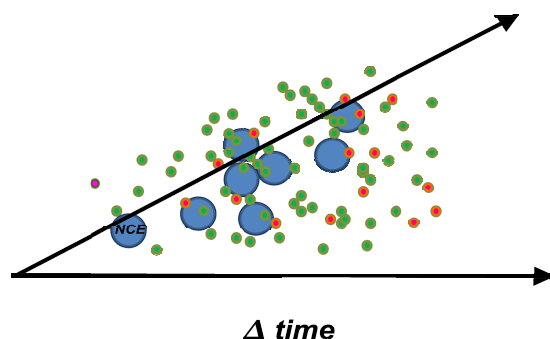
The data, law and policy reviewed in this Article demonstrate that pharmaceutical linkage creates a specific and empirically observable legal nexus between drug approval, drug patents, and patent litigation. This nexus can profoundly shape market entry for brand-name and generic drugs, and thus access to essential medications.

Our work thus far suggests that the scope of this legal nexus depends on at least four discrete mechanisms provided for by law: (1) the type of drug submission; (2) the type of drug patent; (3) the legal standard for patent listing; and (4) how many patents are listed on the patent register. As such, the nexus can be broad (weak) or narrow (specific). The lower the evidentiary standard for new or follow-on drug approval, the easier patents are to come by, the easier it is to list patents on the patent register, and the more patents that can be listed on the patent register, the weaker the legal nexus between approval and patenting.

The discrete legal mechanisms underpinning the linkage regime as they operate in tandem with the evidentiary requirements for drug approval appear to provide an excellent vehicle for the development of

*product clusters*. An example of one such cluster, the focus of our group's current research, is provided in Fig. 7, which presents a recasting of the patent tree data illustrated in Fig. 1 to include a time element.

Product clusters are hypothesized to be comprised of an ever-expanding number of follow-on drugs centered on a single new and original drug. Products in the cluster are surrounded by a halo of patents, all of which are interconnected between products within a given cluster. These patents serve two primary functions. First, they provide support for follow-on drug development within in the cluster, and second they provide fodder for listing on the patent register to delay generic entry on the original new and innovative drug. The greater the number of patents permitted to be listed on the patent register and the greater the scope of patent classifications per patent, the greater the ability of patents to support a product cluster and thus to delay generic entry.



**Fig. 7. Hypothetical Linkage-Based Product Cluster.** Product clusters begin at some point in time with the first new and innovative drug (●; NCE) and associated originating patent (●). With time, and vetting by the market and regulators, further follow-on drug approvals (●) and patents (●) are granted within the cluster, following which an increasing number of patents are listed on the patent register (●). Listed patents can, increasingly, over time, be used to prohibit generic entry on older drugs in the cluster.

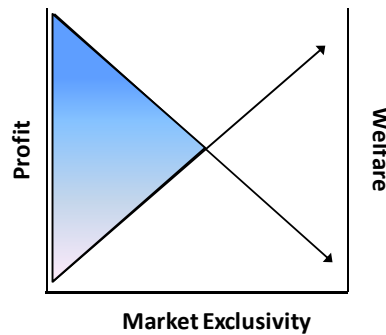
Clearly different clusters will have different spatio-temporal characteristics, for example whether they represent clustering within or between brand-name firms or whether there is a single or small number of truly new and innovative drugs per cluster, but the clustering effect of follow-on drugs and associated patents over time remains a central theme.

Perhaps most important for policy-makers, it may be the *sum* of the interactions between multiple drugs and multiple patents in clusters that most effectively chills generic entry. For this reason it would be very

valuable to develop a working model of innovation that would identify functional linkages between different drugs, patents, and listed patents, and how these linkages combine (and re-combine) over time to delay generic entry. The goal of work underway by our group, parallel to three-dimensional models of protein folding, is to convert data such as that shown in Figs. 1 and 7 into a series of 3-D models that will allow politicians, law-makers, the judiciary, and scholars to track the evolution of clusters over time, both with regard to their structure and function. In this manner, rotational 3-D cluster models would enable visual and numerical quantification of the impact of clustering on generic entry in the same manner that one might look at a car from behind (highlighting the “gas tank,” or original drug product and associated patent tandems) as well as from the side (from the rear to the front of the vehicle, underscoring how and when approvals, patents, and listed patents increase over time with market and regulator vetting).

In a best case scenario, data such as these could be paired with objective evidence of the level of innovation and therapeutic benefit associated with various follow-on drugs in the cluster, allowing for weighted algorithms to be created for pricing and reimbursement purposes. Such algorithms may also provide an evidence-based empirical indicator of the need by governments to fund high-risk research and development activities by pharmaceutical companies.

Product clusters may have particular relevance for loopholes within the linkage regime that allow for what we referred to in our Northwestern study as a “paradoxical approval-patent linkage.” The paradoxical nature of the drug approval-drug patenting nexus refers to the situation where multiple line extensions occur within a cluster that in turn are allowed, via the multiple patent listing provision, to extend market exclusivity on the original new drug form, but also all other chemically-related drug forms against which they may be listed on the patent register over time.



**Fig. 8. Paradoxical Drug Approval-Drug Patenting Nexus.** Left and right axes represent increases (profit) and decreases (welfare) in firm profits and public welfare resulting from an increase in market exclusivity associated follow-on drug product clusters as the number of line extensions and cumulative patent protection for the product cluster increase. Both profit and public welfare are assumed for the sake of simplicity to change linearly from the origin. The upward arrow represents profit whereas the downward arrow represents public welfare. The graph indicates that increases in the duration of market exclusivity (and hence monopoly pricing) on drug clusters with little public welfare benefit yield an increasingly paradoxical relationship between the scope of patent protection per cluster and the degree of social benefit associated with that protection.

As illustrated in Fig. 8, as the number of follow-on drugs in the cluster grows over time so too does cumulative market exclusivity and firm profit. The maximum point of inefficiency (or the most ‘paradoxical’ drug approval-drug patenting nexus) occurs when the product cluster has a very long duration of cumulative market exclusivity with little or no therapeutic benefit to the larger population compared with the original pioneering drug on which the cluster is based. Given that empirical data are only beginning to be reported, this clustering effect may present a more substantial barrier to generic entry than previously recognized, and it is not clear whether generics are being adequately compensated for taking on the risk of litigation.

A critical element of empirical work done by us and/or other groups going forward should be to assess clustering data before and after critical amendments to linkage laws, such as those aimed at reducing the automatic stay from many to one per reference product and narrowing the scope of listable patents from those generally on a marketed drug to those only relevant to the specific drug submission against which they are listed.

### *B. Globalization of Pharmaceutical Linkage*

As discussed at the beginning of the Article, prompt and affordable access to essential medicines is a significant component of most domestic and global models of public health. The availability and costs



of new and generic drugs is a function of traditional patent law incentives and emerging linkage regulations.<sup>160</sup> Patent law is a well described,<sup>161</sup> if controversial,<sup>162</sup> “policy lever” for stimulating the development of new drugs.<sup>163</sup> As discussed throughout this Article, linkage regulations tie generic drug availability to existing drug patents by connecting approval to the resolution of patent validity or infringement,<sup>164</sup> potentially resulting in long and costly litigation.<sup>165</sup> While the patent system has been in operation for about 500 years,<sup>166</sup> the linkage regime has only been in existence for about 25 years following passage of the Hatch-Waxman Act in the United States in 1984<sup>167</sup> and

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160. For an account of the relationship between patents and drug discovery, development, and marketing from the earliest days of the industry to the present, see generally GRAHAM DUTFIELD, *INTELLECTUAL PROPERTY RIGHTS AND THE LIFE SCIENCE INDUSTRIES: PAST, PRESENT AND FUTURE* (2d ed. 2009).

161. See generally BENGT DOMEIJ, *PHARMACEUTICAL PATENTS IN EUROPE* (2000); Bengt Domeij, *Initial and Follow-on Pharmaceutical Inventions in Europe*, in *ECONOMICS, LAW AND INTELLECTUAL PROPERTY* 177•98 (2003). See also Kenneth Arrow, *Economic Welfare and the Allocation of Resources for Innovation*, in *THE RATE AND DIRECTION OF INVENTIVE ACTIVITY* 609•26 (1962); *INTELLECTUAL PROPERTY RIGHTS: CRITICAL CONCEPTS IN LAW* (2006); Dan L. Burk & Mark A. Lemley, *Policy Levers in Patent Law*, 89 *Va. L. Rev.* 1575 (2003); Robert P. Merges & Richard R. Nelson, *On the Complex Economics of Patent Scope*, 90 *COLUM. L. REV.* 839 (1990).

162. See generally KRIMSKY, *supra* note 8; BOLDRIN & LEVINE, *supra* note 9; Jaffe, *supra* note 10; Mazzoleni & Nelson, *supra* note 10; ANGELL, *supra* note 7; Kevin Outterson, *Pharmaceutical Arbitrage: Balancing Access and Innovation in International Prescription Drug Markets*, 5 *YALE J. HEALTH POL'Y L. AND ETHICS* 193 (2005); Michele Boldrin & David K. Levine, *The Economics of Ideas and Intellectual Property* STAFF REPORT 357 (Federal Reserve Bank Of Minneapolis, Minneapolis, M.N.) Feb. 2005, at 102 [hereinafter *Economics of Ideas*]; Keith Pavitt, *Proceedings of the National Academy of Sciences of the United States of America National Policies for Technical Change: Where are the Increasing Returns to Economic Research?*, 93 *PROC. NAT'L ACAD. SCI.* 126 (1996).

163. Ron A. Bouchard, *Should Scientific Research in the Lead-Up to Invention Vitate Obviousness Under the Patented Medicines (Notice Of Compliance) Regulations: To Test or Not to Test?*, 6 *CAN. J.L. & TECH.* 1, 1–27 (2007) [hereinafter Bouchard 2007a]; Bouchard 2007b, *supra* note 143; Bouchard KSR Part 1, *supra* note 119, at 222–46; Thomas Faunce & Joel Lexchin, *'Linkage' Pharmaceutical Evergreening in Canada and Australia*, 4 *AUSTL. AND N.Z. HEALTH POL'Y* 1, 8 (2007); Paul Jones, *KSR and the Supreme Court: The Silence is Deafening*, 53 *ANTITRUST BULLETIN* 849 (2008).

164. For a review of Canadian linkage regulations, see *infra* part I. See also Bouchard 2010, *supra* note 13, at 174–227; Bouchard 2009, *supra* note 14; Monica Sawicka & Ron A. Bouchard, *Empirical Analysis of Canadian Drug Approval Data 2001–2008: Are Pharmaceutical Players “Doing More with Less”?*, 3 *MCGILL J.L. & HEALTH* 85, 109 (2009); Joel Lexchin, *After Compulsory Licensing: Coming Issues in Canadian Pharmaceutical Policy and Politics* 40 *HEALTH POL'Y* 69 (1997).

165. *Economics of Ideas*, *supra* note 162.

166. Jean O. Lanjouw & William Jack., Brief, *Trading Up: How Much Should Poor Countries Pay to Support Pharmaceutical Innovation?*, 4 *Ctr. for Global Dev.* 1, 1–8 (2004).

167. 21 U.S.C. § 355(j)(7)(A) (2006) (establishing a list of “Approved Drug Products with Therapeutic Equivalence” commonly known as the “Orange Book”). For a description

the Canadian NOC Regulations in 1993.<sup>168</sup> Importantly, the objective of linkage in both originating jurisdictions was to balance the competing policy goals of stimulating the development of new and innovative drugs and the timely entry of generic drugs.<sup>169</sup>

Compared to the patent system, the linkage regime thus represents a novel and emerging intellectual property paradigm for protecting pharmaceutical inventions. Even so, by 2010, we are witnessing the rapid spread of the linkage regime on a global level, due largely to a growing number of multilateral and bilateral free trade agreements with the U.S.<sup>170</sup> These agreements often require participating nations to incorporate linkage and other intellectual property provisions in exchange for preferential trade terms.<sup>171</sup> As many such agreements are negotiated outside the purview of the World Trade Organization (WTO) and provide stronger intellectual property protection for drugs than does TRIPS, they are often referred to as “TRIPS-Plus”.<sup>172</sup> Suggestive of the strength of the multinational pharmaceutical lobby, the European Commission (E.C.) has recently reported numerous instances where member nations have attempted to institute pharmaceutical linkage regimes even though E.U. law prohibits this

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of U.S. linkage laws, see Gerald Mossinghoff, *Overview of the Hatch-Waxman Act and Its Impact on the Drug Development Process*, 54 FOOD & DRUG L.J. 187–94 (1999); Caffrey & Rotter, *supra*, note 155, at 4–7; Rebecca S. Eisenberg, *Patents, Product Exclusivity, and Information Dissemination: How Law Directs Biopharmaceutical Research and Development*, 72 FORDHAM L. REV. 477, 483 (2003); Jeremy Bulow, *The Gaming of Pharmaceutical Patents*, in 4 INNOVATION POL’Y AND THE ECONOMY: NAT’L BUREAU OF ECON. RES. (2004); Epstein & Kuhlik, *supra* note 90; Mathew Avery, *Continuing Abuse of the Hatch-Waxman Act by Pharmaceutical Patent Holders and the Failure of the 2003 Amendments*, 60 HASTINGS L.J. 171 (2008–2009).

168. Patented Medicines (Notice of Compliance) Regulations SOR/1993-133 (Can.). For early descriptions of Canadian linkage law, see, e.g., Tancer, *supra* note 4; Harrison, *supra* note 4; Hore, *supra* note 155.

169. Avery, *supra* note 167; Bouchard 2010, *supra* note 13.

170. Carlos María Correa, *Implications of Bilateral Free Trade Agreements on Access to Medicines*, 84 BULL. OF THE WORLD HEALTH ORG. 399–404 (2006); Judit Rius Sanjuan, *Patent-Registration Linkage*, DISCUSSION PAPER – NO. 2 (Consumer Project on Tech.), Apr. 3, 2006, at 1, <http://www.cptech.org/publications/CPTechDPNo2Linkage.pdf>; Overview on Patent Linkage, CONSULTING REPORT, (Finston Consulting, LLC, Washington D.C.) Aug. 7, 2006, at 1, available at, <http://www.finstonconsulting.com/version03/files/Overview.pdf> (UK Consulting Report).

171. Tomas Alured Faunce, *Global Intellectual Property Protection for Innovative Pharmaceuticals: Challenges for Bioethics and Health Law*, in GLOBALISATION AND HEALTH 87–108 (2006); Tomas Alured Faunce & Kathy Shats, 62 *Bilateral Trade Agreements as Drivers of National and Transnational Benefit From Health Technology Policy: Implications of Recent US Deals for Australian Negotiations with China and India*, AUSTL. J. OF INT’L AFF. 196–213 (2008).

172. Correa, *supra* note 170, at 401.

form of intellectual property law.<sup>173</sup>

The implications of pharmaceutical linkage for global public health are immense. As reviewed in Section I above, there is growing empirical evidence to suggest that pharmaceutical linkage can substantially extend cumulative patent terms for high value drugs.<sup>174</sup> These results are consistent with early predictions of the impact of linkage regulations by Schondelmeyer,<sup>175</sup> based on his work with the originating U.S. regime.<sup>176</sup> An additional concern is that the extension of market exclusivity on brand-name drugs occurs even though up to 75% of the patents challenged on the merits may be invalid or not infringed by the generic equivalent.<sup>177</sup> Pharmaceutical linkage creates a conflicting system where governments with linkage regimes that limit the timely appearance of generics also depend on these firms to produce cost savings and limit the growth in pharmaceutical expenditures.<sup>178</sup> A related issue is that costs of prolonged litigation are known to be passed

173. *European Comm'n Pharm. Sector Inquiry*, FINAL REP. (EC) July 8, 2009, at 23 [hereinafter FINAL REP.]. This theme is developed extensively in the European Commission Pharmaceutical Sector Inquiry Preliminary Report. See *European Comm'n Pharm Sector Inquiry*, PRELIMINARY REP. (EPO). OCT. 3, 2008, at 14, 113 [hereinafter PRELIMINARY REP.].

174. Bouchard 2009, *supra* note 14.

175. Dr. Stephen Schondelmeyer, a pharmacologist and health economist, gave evidence before the House of Commons to the effect that it is not the term of single patents that mattered most, but rather how patents add cumulatively to extend market exclusivity, a claim the government at the time vigorously denied. Compare testimony of Dr. Stephen Schondelmeyer (Professor, University of Minnesota) and Dr. Elizabeth Dickson (Director General, Chemical and Bio-Industries Branch, Department of Industry, Science and Technology). *Minutes of Proceedings and Evidence of the Legislative Committee on Bill C-91*, 34:7 Parliament of Canada, 7:65–7:96 (Dec. 1, 1992); *id.* at 34:8 Parliament of Canada, 8:37–8:40 (Dec. 1, 1992).

176. Lara J. Glasgow, *Stretching the Limits of Intellectual Property Rights: Has the Pharmaceutical Industry Gone Too Far?*, 41 *Idea* 227, 233 n.27 (2001) (citing The Gale Group, *Intellectual Property Rules: A Delicate Balancing Act for Drug Development*, 23 *CHAIN DRUG REV.*, RX13 (2001)).

177. *Generic Drug Entry Prior to Patent Expiration*, FTC STUDY (Fed. Trade Comm'n), July 2002, <http://www.ftc.gov/os/2002/07/genericdrugstudy.pdf>, [hereinafter F.T.C. Study 2002]. See Hore, *supra* note 155; Caffrey & Rotter, *supra* note 155, at 40 n.293. It should be noted, however, that these data are now somewhat old, and require updating in both the United States and Canada following amendments to the respective linkage regimes over the last half decade.

178. PRELIMINARY REP., *supra* note 173, at 314. The European Commission states: Originator companies may also litigate against pricing and reimbursement bodies, claiming patent infringement, irregularities in the generic registration file or concerns about bioequivalence or non-compliance of the promotional material. However, as described in Chapter C.2.5., when the interventions before the marketing authorisation [sic] authorities lead to litigation, originator companies lose most of the cases, which suggest that the arguments submitted against the generic product could not be substantiated.

on to consumers,<sup>179</sup> with differential costs to governments and the public in accordance with their system of drug reimbursement,<sup>180</sup> public health,<sup>181</sup> public-private discourse,<sup>182</sup> and health equity.<sup>183</sup>

Considerations such as the forgoing must, of course, be balanced against the widely accepted need for innovative drugs in developed and developing nations, the presumption favoring the validity of patents in most developed nations,<sup>184</sup> as well as, the notion in law that if the state grants a party an exclusive right, it cannot grant another party permission to invade that right without just cause. For this reason the twin policy goals underpinning linkage are said to be “competing” in nature.

In addition to shaping the marketplace for brand-name and generic drugs, intellectual property protection for pharmaceuticals, including linkage, has become a controversial cog in the global machine of providing individuals with essential medications, including in developed<sup>185</sup> and developing<sup>186</sup> nations. Canada, like many developed

179. BOLDWIN & LEVINE, *supra* note 9; Bulow, *supra* note 167.

180. EXPLORING SOCIAL INSURANCE: CAN A DOSE OF EUROPE CURE CANADIAN HEALTH CARE FINANCE? (Colleen Flood, Mark Stabile & Carolyn Tuohy, eds., 2008); CANADIAN HEALTH LAW AND POLICY, (Colleen Flood, Mark Stabile & Carolyn Tuohy, eds., 3d ed. 2007); JUST MEDICARE: WHAT'S IN, WHAT'S OUT, HOW WE DECIDE (Colleen Flood, ed. 2006); ACCESS TO CARE, ACCESS TO JUSTICE: THE LEGAL DEBATE OVER PRIVATE HEALTH INSURANCE IN CANADA (Colleen Flood, Kent Roach & Lorne Sossin, eds. 2005).

181. HILTS, *supra* note 7; AVORN, *supra* note 7; ANGELL, *supra* note 7; COHEN, *supra* note 7; RAY MOYNIHAN & ALAN CASSELS, SELLING SICKNESS: HOW THE WORLD'S BIGGEST PHARMACEUTICAL COMPANIES ARE TURNING US ALL INTO PATIENTS (2005).

182. Mary E. Wiktorowicz, *Emergent Patterns in the Regulation of Pharmaceuticals: Institutions and Interests in the United States, Canada, Britain, and France*, 28 J. HEALTH POL. POL'Y & L. 615, 620 (2003).

183. See *Integrating Intellectual Property Rights and Development Policy*, REP. (World Health Org.), 2006; Eric Noehrenberg, *Report of the Commission on Intellectual Property Rights, Innovation and Public Health: An Industry Perspective*, 84 BULL. OF THE WORLD HEALTH ORG., May 2006, at 419; Emmanuel Hassan, Ohid Yaqub, & Stephanie Diepeveen, *Intellectual Property and Developing Countries*, RAND CORP. (2010); Kevin Outterson, *Should Access to Medicines and TRIPS Flexibilities Be Limited to Specific Diseases?*, 34 Am. J.L. & Med. 279, 279-301 (2008). See generally Trudo Lemmens, *Leopards in the Temple: Restoring Scientific Integrity to the Commercialized Research Scene*, 32 J.L. MED. & ETHICS 641 (2004); Trudo Lemmens, *Piercing the Veil of Corporate Secrecy about Clinical Trials*, HASTINGS CTR. REP., (2004) 14; E. Richard Gold, *The Reach of Patent Law and Institutional Competence*, 1 OTTAWA L. & TECH. J. 263 (2004).

184. For a critique of the presumption of validity in patent law, see Mark A. Lemley & Douglas Lichtman, *Rethinking Patent Law's Presumption of Validity*, 60 STAN. L. REV. 45 (2007).

185. Aaron S. Kesselheim & Jeffery Avorn, *Biomedical Patents and the Public's Health: Is There a Role for Eminent Domain?*, 295 JAMA 434, 434-37 (2006).

186. *Public Health: Innovation and Intellectual Property Rights*, REP. OF THE COMM'N

nations, has attempted to play a key role in the global effort to provide underserved populations with essential medications through its Access to Medicines Regime,<sup>187</sup> but with less success than anticipated.<sup>188</sup> Moreover, and perhaps more importantly, up to this point effort has been focused primarily on the limits of traditional patent law,<sup>189</sup> with emerging forms of patent and other regulatory protection receiving considerably less attention.

A related observation is that while the concept of pharmaceutical linkage is relatively new compared to the patent system, there is already significant pressure to broaden it beyond drug approval to include linkage between patent rights and other regulatory aspects of drug approval and marketing.<sup>190</sup>

One of the major implications of the empirical research reviewed from Studies 1, 2, and 3 is that inclusion of linkage in a nation's basket of international trade obligations may present a more expansive notion of patent protection for drug products than previously recognized, particularly when gauged against the relatively narrow nexus originally envisaged between drug patents and the marketed products against which they are listed.<sup>191</sup> For example, the E.C. Pharmaceutical Sector Inquiry<sup>192</sup> has articulated a broad definition of pharmaceutical linkage,

ON INTELL. PROP. RIGHTS, INNOVATION AND PUB. HEALTH (World Health Org., Geneva, Switzerland), April 25, 2006; Graham Dutfield, *Delivering Drugs to the Poor: Will the TRIPS Amendment Help?*, 34 AM. J. L. & MED. 107-24 (2008); Aaron Kesselheim, *Think Globally, Prescribe Locally: How Rational Pharmaceutical Policy in the U.S. Can Improve Global Access to Essential Medicines*, 34 AM. J. L. & MED. 125, 125-139 (2008).

187. Canada's Access to Medicines Regime was established by the Government of Canada. It allows Canada to enact *compulsory licenses*, despite provisions in the Patent Act to the contrary, to export *essential medicines* to countries without capacity to manufacture the same. The popular front for this effort was the 2004 Act to amend the Patent Act and the Food and Drugs Act, also known as the Jean Chrétien Pledge to Africa Act. For more information see CANADA'S ACCESS TO MEDICINES REGIME, [http://www.camr-cam.gc.ca/index\\_e.html](http://www.camr-cam.gc.ca/index_e.html) (last visited Oct. 18, 2010).

188. Jillian Clare Kohler et al., *Canada's Access to Medicines Regime: Promise or Failure of Humanitarian Effort?*, 5 HEALTHCARE POL'Y 40, 40-48 (2010).

189. Peter Drahos, *Intellectual Property and Pharmaceutical Markets: A Nodal Governance Approach*, 77 Temp. L. Rev. 401, 401-424 (2004); THE POWER OF PILLS: SOCIAL, ETHICAL AND LEGAL ISSUES IN DRUG DEVELOPMENT, MARKETING AND PRICING (Jillian Clare Cohen, Patricia Illingworth & Udo Schulenk eds., 2006).

190. FINAL REP., *supra* note 173; PRELIMINARY REP., *supra* note 173.

191. Caffrey & Rotter, *supra* note 155; Hore, *supra* note 155; Bouchard 2009, *supra* note 14.

192. FINAL REP., *supra* note 173. In the Executive Summary, the E.C. states that: The Commission will continue to strictly enforce the applicable Community law and, for instance, act against patent linkage, as according to Community legislation, marketing authorisation [sic] bodies cannot take the patent status of the originator medicine into account when deciding on marketing authorisations [sic] of generic

including linkage of patent status to the following: formal legal proceedings between parties, patent settlements, interventions before national drug regulators regarding market approval, drug pricing, and reimbursement.<sup>193</sup> An evolving landscape such as this raises the question of whether the pharmaceutical industry is using linkage as an emerging stepping-stone in its efforts to control the movement of drugs across international borders. Moreover, a growing number of legal disputes have been reported whereby countries without linkage regulations have attempted to import or export drugs where shipments are seized by other nations alleging that these shipments are in violation of domestic patent laws linked to international trade instruments,<sup>194</sup> such as TRIPS or other FTAs.<sup>195</sup>

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medicines.

*Id.* at 23.

In the 2008 Preliminary Report, the E.C. stated more specifically that patent-linkage is considered unlawful under Regulation (EC) No 726/2004 and Directive (EC) No 2001/83. PRELIMINARY REP., *supra* note 173, at 14. Further elaboration is provided to the effect that:

Patent linkage refers to the practice of linking the granting of MA, the pricing and reimbursement status or any regulatory approval for a generic medicinal product, to the status of a patent (application) for the originator reference product. Under EU law, it is not allowed to link marketing authorisation [sic] to the patent status of the originator reference product. Article 81 of the Regulation and Article 126 of the Directive provide that authorisation [sic] to market a medicinal product shall not be refused, suspended or revoked except on the grounds set out in the Regulation and the Directive. Since the status of a patent (application) is not included in the grounds set out in the Regulation and in the Directive, it cannot be used as an argument for refusing, suspending or revoking MA.

*Id.* at 113–14.

193. PRELIMINARY REP., *supra* note 173, at 22–23. The report states:

Interventions before regulatory bodies (marketing authorisation [sic] authorities and pricing and reimbursement bodies) appear to be a standard tool in originator companies' toolbox. Although contacting the health authorities may address legitimate concerns, it can also be used to delay or block the marketing authorisation [sic] or the pricing or reimbursement status of the generic product. In particular, by suggesting that the generic product is less efficient or safe or is not equivalent, raising patent infringement issues concerning the generic product in question and alleging that any decision favourable [sic] to the generic company would make the authorities liable to patent infringement damages (patent linkage), originator companies gain time and can create delays in granting marketing approval for the generic product and its entry into the market.

*Id.* at 314.

194. See NAFTA, *supra* note 2; TRIPS, *supra* note 2.

195. For example, a 2008 shipment of the anti-HIV drug Abacavir was confiscated by Dutch customs authorities. The shipment was from an Indian company bound for Nigeria. It was paid for by UNITAID, the drug purchase arm of the WHO and was meant to be distributed by the William J. Clinton Foundation. See, e.g., Posting of GenericIPguy to Indian Patent Oppositions: Abacavir Hemisulfate - Indian pre grant opposition documents, <http://indianpatentoppositions.blogspot.com/2007/11/abacavir-hemisulfate-indian-pre->

Owing to the confluence of the events reviewed above over time, linkage regulations in respect to therapeutic products have quietly emerged as key driver of public health costs and medical product regulation on the global stage, both for developed and developing nations.

The Author is a member of a new global consortium of intellectual property and health policy scholars, economists, and practicing lawyers in nine counties (Consortium), who have come together to study global pharmaceutical linkage regulation.<sup>196</sup>

When the Consortium began its work, the obvious question to ask was—what should the focus be of future research on pharmaceutical linkage as it evolves globally away from its North American roots? In its work thus far,<sup>197</sup> the Consortium recognizes that the study of structure-function relationships in living systems, both at the micro and macro level, has served empirical science especially well over the last century. Indeed, the rapid spread of pharmaceutical linkage worldwide offers a unique and time sensitive opportunity to carry out empirical work on the system as it evolves globally from its point of origin in the United States. A major goal of our work on global pharmaceutical linkage will be to investigate the structural and functional aspects of different systems of linkage regulations in different jurisdictions, and their relationship on the one hand to drug availability costs, and expenditures, and incentives for innovation and protection of intellectual property rights on the other.

Key decision makers, pharmaceutical firms, the courts, patent counsel, consumers, and other actors are assumed to interact in

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grant.html (last visited Nov. 21, 2007, 02:24); EUR-Lex - 32003R1383-EN, <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=CELEX:32003R1383:EN:HTML> (last visited Oct. 18, 2010 02:14).

196. The consortium is spread across nations with mature linkage regulations (United States and Canada), nascent regulations (Australia and China), those without regulations but with certain practices that may operate to parallel linkage (E.U.), and those where both the existence and scope of linkage regulations are currently the subject of intense public scrutiny and litigation (India, Mexico, and South Korea). It includes individuals with past and present litigation experience with pharmaceutical regulations on both sides of the brand-generic divide, and includes scholars appointed in faculties of law, medicine, health, and economics as well as practicing lawyers working in law firms and non-governmental organizations on pharmaceutical matters. The consortium is fortunate to be supported in its endeavors by a Key Decision Maker Advisory Board (KDM<sub>AB</sub>) composed of senior members of government in health, industry, and intellectual property portfolios and the judiciary working on matters relating to pharmaceutical linkage regulations.

197. Bouchard, R.A. Cahoy, D., Domeij, B., Dutfield, G., Faunce, T., Hollis, A., Jones, P., Ali Khader, F., Lexchin, J., Nam, H., & Serrano, J.L. "Global Pharmaceutical Linkage Regulations: A Consortium Framework." *Minnesota Journal of Law, Science & Technology* 12(2): 1-30. 2011.

domestic and global networks through reasonably well-defined channels of communication.<sup>198</sup> As in other complex political and economic systems,<sup>199</sup> this network is assumed to have structural and functional characteristics that can be identified and measured, and which in turn serve as appropriate benchmarks to assess the performance of the system relative to its goals and objectives.

The specific basket of legal checks and balances in a given linkage regime is pivotal, as it determines not only how a complex system of pharmaceutical regulation begins operating *de novo* following the coming into force of law but also, how it evolves over time to yield demonstrable empirical results. It has been previously shown, for example, that the behavior of dynamic legal systems,<sup>200</sup> including how systems learn, self-regulate, and adapt and grow,<sup>201</sup> is strongly influenced by positive and negative feedback.<sup>202</sup> Positive feedback is feedback that results in growth or amplification of a particular process or group of related processes whereas negative feedback results in tamping or slowing of a particular process or group of processes. Studies of complex social, biological, and technological systems have shown that the unintended consequences resulting from feedback has the potential to force a system away from operating at or near the point of efficiency.<sup>203</sup>

We have used the term “structural” to refer to the broad administrative, legal, and policy attributes of the linkage regime in differing jurisdictions as these represent the initial starting conditions for operation of local linkage regimes. The initial starting conditions, as

198. Drahos, *supra* note 189.

199. Harrison, *supra* note 4; JERVIS, *supra* note 32; Bozeman & Sarewitz, *supra* note 81; Bozeman, *supra* note 81; Sterman, *supra* note 80.

200. Neil E. Harrison, *Thinking About the World we Make, in* COMPLEXITY IN WORLD POLITICS: CONCEPTS AND METHODS OF A NEW PARADIGM 1, 10 (Neil E. Harrison ed., 2006) [hereinafter COMPLEXITY]; JERVIS, *supra* note 32.

201. See, e.g., J.B. Ruhl, *The Fitness of Law: Using Complexity Theory to Describe the Evolution of Law and Society and its Practical Meaning for Democracy*, 49 VAND. L. REV. 1407 (1996); J.B. Ruhl, *Regulation by Adaptive Management: Is It Possible?*, 7 MINN. J.L. SCI. & TECH. 21 (2005–2006).

202. Feedback interactions in complex systems have received increased attention in recent years. See generally Barabási, *supra* note 142; Gleick, *supra* note 142; Holland 1992, *supra* note 142; Holland 1995, *supra* note 142; Johnson, *supra* note 142; Kauffman, *supra* note 142; Nicolis & Prigogine, *supra* note 142; Waldrop, *supra* note 142; Arthur, *supra* note 142, at 92–99.

203. See, e.g., Robert M. May et al., *Complex Systems: Ecology for Bankers*, 451 NATURE 893 (2008). For a look at the role of feedback in policy failure, see generally JERVIS, *supra* note 32; COMPLEXITY, *supra* note 200; Bozeman, *supra* note 81; Bozeman & Sarewitz, *supra* note 81; and Sterman, *supra* note 80.



in dynamical physical systems,<sup>204</sup> represent the sum of the political, economic, and public policy conditions that together form the “take-off” point for a new law and the conditions in which it begins to operate. The structural aspect also encompasses the specific legal mechanisms that drive operation of linkage regimes in various jurisdictions. Identifying the structural attributes and mechanisms of individual linkage systems is important, as they provide the benchmark from which to assess the successes and failures of each system in operation and their potential to combine to form a global regulatory regime. By contrast, we use the term “functional” to refer to the outputs of the regulations in each jurisdiction as well as how they functionally interact across borders to operate as a global regulatory regime. The functional aspects of a system reflect the behavior of the system as it evolves with time away from the initial starting conditions.<sup>205</sup>

A significant advantage of a globally-based Consortium approach to the study of pharmaceutical linkage is that studying linkage in different jurisdictions allows for both an investigation of the structural and functional characteristics of local linkage regimes with different initial starting conditions and different legal mechanisms of operation, the identification of general rules of linkage as the different national forms of linkage interact and influence global pharmaceutical regulation. The former provides a *descriptive* mechanism for assessing the successes and failures of different regimes, while the latter provides a *prescriptive* approach for key decision makers to revise, institute, or abolish linkage regulations according to the goals and objectives of differing nations.

The goal of the Consortium’s future work on global pharmaceutical linkage is to produce and use empirical knowledge relating to the structure and function of different linkage regimes as a knowledge translation tool for assessing the strengths, weaknesses, successes, and failures of pharmaceutical linkage in individual nations and as they combine to form a global system of pharmaceutical linkage. A secondary goal is to directly assist key decision-makers and knowledge users in domestic and global governments and legal systems working

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204. See generally Barabási, *supra* note 142; Gleick, *supra* note 142; Holland 1992, *supra* note 142; Holland 1995, *supra* note 142; Johnson, *supra* note 142; Kauffman, *supra* note 142; Nicolis & Prigogine, *supra* note 142; Waldrop, *supra* note 142; Arthur, *supra* note 142, at 92–99.

205. COMPLEXITY, *supra* note 200; JERVIS, *supra* note 32; see also, Clifford Shearing & Jennifer Wood, *Nodal Governance, Democracy, and the New ‘Denizens,’* 30 J.L. & SOC’Y 400, 401–06; LES JOHNSTON & CLIFFORD SHEARING, *GOVERNING SECURITY: EXPLORATIONS IN POLICING AND JUSTICE* ch. 8, 138 (2003); Scott Burris, *Governance, Microgovernance and Health*, 77 TEMP. L. REV. 335, 357 (2004); Drahos, *supra* note 189.

with linkage regimes in their efforts to stimulate the production of new and innovative drugs while at the same time lowering public health costs and increasing access to essential medicines.

#### SUMMARY & CONCLUSIONS

Our empirical investigation into the nexus between drug approval, drug patenting, patent listing, and litigation under the domestic Canadian linkage regime for pharmaceuticals has yielded a number of important observations. Primary among these is that the development, approval, and marketing of new and innovative breakthrough drugs have stagnated in favor of follow-on drug development. The number of truly innovative drugs is very low, representing about 1.87% of all brand-name submissions and 1.23% of total submissions. This trend has been ongoing for about a decade and appears to have occurred independent of concomitant changes in firm patenting, patent listing, and patent litigation. The second primary observation is that operation of the linkage regime over the same timeframe has resulted in a doubling of cumulative patent protection for blockbuster drugs, from an average term of twenty-two years to a term of forty-three years. Extended patent protection under the NOC Regulations was associated with a substantial degree of litigation, often resulting in opposing decisions on validity or infringement at the same level of court. Unlike the U.S. linkage regime, litigation in Canada is deemed to be judicial review in nature. Thus generic firms, while successful on issues of validity or infringement under linkage laws, remain vulnerable to a post hoc infringement action. There is little question as to whether these costs are passed on to consumers in the form of monopoly prices. Together the data show that the production of new and innovative drugs is low and decreasing over time, domestic pharmaceutical companies are focused more on appropriating existing technologies than on breakthrough drug development, and that generic entry on high value drugs is being increasingly delayed.

The empirical findings reviewed here are at odds with the intent of the federal government in enacting the NOC Regulations to stimulate the development of new and innovative drugs and facilitate the timely entry of generic drugs. Questions as to the validity of the NOC Regulations arise when a purposive patent-specific approach to interpreting the NOC Regulations is taken, as stipulated by the Supreme Court of Canada in its leading patent jurisprudence. Taking this approach to analysis of the linkage of drug approval and drug patenting in the specific infringement context of Section 55.2(1) of Canada's Patent Act, one could argue that the concept of early working

does not refer to the working of *any* patent at *any* time. As suggested by testimony by the federal government before the Legislative Committee on Bill C-91, the early working provision was intended to refer to a specific patent on a specific drug so as to allow generic firms to prepare for timely market entry in relation to that drug and that patent. A second element of a patent-specific analysis is that a drug referred in Section 55.2(1) is not a new and innovative drug for the purposes of *all* time. It is a drug that is new and innovative at a particular time in history. The moment when this drug is no longer new or innovative, for example when it becomes the basis of SNDS submissions and follow-on drugs, constitutes the moment in history when patents are no longer in relation to new and innovative drugs, and thus, the moment which may reasonably trigger timely generic entry.

A similar conclusion may be drawn from the legal debate surrounding the coming into force of the U.S. Hatch-Waxman regime, particularly with respect to influential reports from the Committee on Energy and Commerce and the Committee on the Judiciary preceding the legislation.

Relegating listing only to specific drug submissions considered to be “new and innovative” based on objective evidence rather than in an arbitrary manner on all new (NDS) and follow-on (SNDS) submissions, would be in line with the spirit of the regulations to encourage the development of new and innovative drugs and to facilitate the timely entry of generic alternatives. The same is true of the multiple patent listing model, whereby listings could be pruned by regulators only to the small number of patents associated with demonstrably new and innovative drugs. Amendments such as these would accord with the framework for the linkage regime put forward by the Canadian government in the lead-up to Bill C-91 as well as reports by the Committee on Energy and Commerce and the Committee on the Judiciary in the United States in the lead-up to Hatch Waxman. At the time both pieces of legislation came into force, U.S. and Canadian governments strongly asserted that linkage protection was aimed at a narrow range of patents on new and innovative drugs, and when that narrow range of patents expire, anyone in a position to copy that product can legally bring it to market. As discussed above in greater detail, the language used by both governments is consistent with the plain meaning of the terms “new and innovative” and “timely.”

In choosing the words “the development of new and innovative drugs” to be one-half of the balance linking patent law to food and drug law, federal governments in the United States and Canada articulated a clear public policy goal that pioneering drug development is desired in

exchange for the “unusual protections” afforded to the pharmaceutical industry by the linkage regime. Similarly, in choosing the words “timely market entry of their lower priced generic competitors” these governments articulated a second public policy goal of cost savings, triggered by expiry of specific patents on specific drug forms that are no longer new and innovative. Thus the balance sought to be effected by pharmaceutical linkage is not just a qualitative balance between poles, but also a quantitative balance. The more reward there is on the private side of the ledger, the more there must be on the public side in order to maintain a valid legal equilibrium.

The data in Studies 1, 2, and 3 demonstrate that, when analyzed in its “real world” context, the Canadian linkage regulations are not working either as intended by Parliament at the time the law was passed or in a manner that is consistent with the goals and objectives of the federal government as articulated in later RIAS documents. Private firms are obtaining extended patent protection for weakly inventive products, while at the same time generic competition is markedly delayed. The result is that pharmaceutical firms are reaping the rewards of intellectual property protection at historically high levels in this country while the public (and institutional payers) is being deprived of reasonably priced pharmaceuticals.

In light of the principle of statutory interpretation that legislation should be understood and assessed objectively in the setting in which it operates, it is possible that the operation of the NOC Regulations as currently constituted breaches the quid pro quo of the traditional patent bargain from a patent-specific perspective. Based on the same reasoning and evidence one might conclude that the linkage regime does not rectify the mischief it was intended to remedy, and thus may yield a result that is at odds with legislative intent.

Finally, data such as those in Studies 1, 2, and 3 suggest that blending of industrial and health policy goals may be ineffective and possibly counterproductive in terms of public health outcomes. Particularly worrisome is the potential for linkage loopholes permitting a “paradoxical drug approval-drug patenting nexus,” whereby the largest degree of market exclusivity is provided on products with the least amount of innovation. The Article provides a theory of how this may occur within the context of pharmaceutical linkage, via the development of “product clusters.”

There is no question that established and emerging drug regulatory regimes have great potential to increase the efficiency of public health provision by placing both new and innovative and older blockbuster remedies in clinical environments sooner. However, a growing body of

evidence, including data reviewed here, seems to indicate that the efficacy of this approach can be weakened through inadequate monitoring and supervision, such that pharmaceutical firms perceive a higher incentive to exploit existing patented technologies in new ways rather than increasing the flow of new technologies. At a more general level, the data lend empirical substance to an emerging consensus that, in many circumstances, intellectual property rights may be an inhibitor of innovation in so far as this term is construed to yield the greatest social benefits for the public.

It is concluded that policy and legislative incentives designed to stimulate innovation in the pharmaceutical industry have had the opposite effect, and that shifting to a lifecycle regulatory model is unlikely to alter this scenario absent effort to balance economic incentives for breakthrough and follow-on drug development. Importantly, the findings presented in the Article do not suggest unusual behavior by pharmaceutical firms. Rather, the data point to the failure of policy incentives intended to induce the desired result, namely stimulating the development of new and pioneering drugs while also facilitating the timely entry of generic drugs and thus access to essential and affordable medicines.

As discussed in greater detail elsewhere,<sup>206</sup> it is possible that unintended consequences such as those reported here have come about, at least in part, as a result of the discrete system of legal checks and balances comprising the domestic linkage regime, particularly when the balance of “pro-brand” and “pro-generic” provisions in the Canadian system of linkage are compared to those employed in other jurisdictions.

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<sup>206</sup> Bouchard et al. *supra* note 202